THREE ESSAYS ON POTENTIALLY INAPPROPRIATE ANTIDEPRESSANT USE AMONG OLDER ADULTS IN OFFICE-BASED OUTPATIENT SETTINGS

A DISSERTATION
SUBMITTED TO THE FACULTY OF
UNIVERSITY OF MINNESOTA
BY

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IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

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April, 2017

ACKNOWLEDGEMENTS

I would like to thank my family, friends, and dissertation committee for their support and encouragement throughout the process of this dissertation project. Without their continued feedback and insight, I would have not been able to complete my dissertation.

This dissertation is my sole work, and no funding was obtained for the conduct of this study. I own sincere and earnest thankfulness to National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC), which made data publicly available. However, analyses, interpretation, and conclusions do not necessarily reflect the views of the Division of Health Interview Statistics or NCHS of the CDC.

DEDICATION

‘He will wipe every tear from their eyes. There will be no more death’ or mourning or crying or pain, for the old order of things has passed away.” – Revelation 21:4

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CHAPTER 1

Overview: Background and Significance

1.1 Antidepressant and Older Adults

Antidepressants are medications used to treat depressive and other affective/mood disorders, such as anxiety and bipolar disorders.[1,2] Antidepressant use increased nearly 400% from 1988-1994 to 2005-2008 in all ages,[3] and antidepressants were now one of top three most commonly prescribed medications in the U.S.,[4,5] accounting for more than 260 million prescriptions each year.[5] In addition, antidepressants are the ninth most costly medications during the period of 2007-2011 in the U.S., accounting for approximately $20 billion in sales in 2011.[6] Approximately 11% of non-institutionalized U.S. citizens ages 12 and over take antidepressants, and 60% of them have taken antidepressants for two years or longer.[7] Furthermore, antidepressants are disproportionately distributed by age, such that adults ages 40 or older are more likely to take antidepressants than their younger counterparts.[7]

Approximately 15-20% of older adults experience depression in their late life stage, affecting 7 million older adults ages 65 and over in the U.S.[8,9] Late-life depression is a significant public health concern, as depression can increase burden of comorbid conditions (e.g., dementia, diabetes and cardiovascular disease), disability, and mortality among older adults.[10] Unfortunately, older adults are often under-diagnosed and/or under-

treated for depression.[9] When used safely, antidepressants can be an effective pharmacological intervention to treat late-life depression in older adults.

1.2. Potentially Inappropriate Antidepressant Use

Despite the increasing rate of antidepressant use in the general population lately, relatively little is known about the prevalence of and possible reasons for potentially inappropriate use of antidepressants among older adults in office-based outpatient settings. Potentially inappropriate medications are not only continuously prescribed,[11-13] but also remain problematic as they are associated with (1) potentially avoidable healthcare expenditures,[14-16] estimated to be $7.2 billion in a 2001-2002 study,[16] and (2) increased hospitalization,[17-21] morbidity[22] and mortality[20] rates in older adults. Other studies, however, suggest mixed results (e.g., no association between potentially inappropriate antidepressant use and mortality).[23-26] Because avoiding, or reducing, potentially inappropriate use of any medication is an effective strategy to reduce adverse drug events and other medication errors,[11,27] the incidence and/or prevalence of potentially inappropriate medication use may be used as one of the quality of care indicators among older adults in office-based antidepressant-related visits.

In the U.S., a list of potentially inappropriate medications was developed by Beers and his colleagues (hereafter referred to as Beers Criteria) for older adults living in nursing homes in 1991.[28] The Beers Criteria were updated over time[11,29,30] and are now applicable to older adults in all settings of geriatric care.[11] The most up-to-date version of Beers Criteria in 2012 is explicit (i.e., criterion-based) rather than implicit (i.e., judgment-based), as it is based on systematic reviews of clinical studies and expert opinions using

consensus techniques.[11] In particular, it is supported by the American Geriatrics Society (AGS) and Centers for Medicare and Medicaid Services (CMS) among other interest groups.[11] The Beers Criteria are commonly known as the drug-to-avoid criteria (i.e., mis-prescribing as potentially inappropriate medication use), as they focus on the choice of drug and drug interaction. The Beers Criteria are also shown to be appropriate and applicable for research driven by large databases.[11,12] Hereafter, the definition of potentially inappropriate antidepressant use is based on Beers Criteria.

1.3. Epidemiology of Potentially Inappropriate Antidepressant Prescriptions

Monitoring national trends of overall and potentially inappropriate antidepressant prescriptions is important for two reasons. First, as part of the Patient Protection and Affordable Care Act (ACA) of 2010, the *Triple Aim* has been selected as a national strategy to resolve health care issues.[31,32] When applied to older adults who are prescribed with antidepressants in office-based outpatient visits, the *Triple Aim* may consist of: (1) improving patient experience of care (e.g., providing value-based care); (2) improving the health of populations (e.g., reducing adverse drug events); and (3) reducing costs (e.g., reducing avoidable health care expenditures). A descriptive study of patterns for overall and potentially inappropriate antidepressant prescriptions at the national level can be informative as an initial step towards the *Triple Aim*, as it can further shape future research and practice guidance to achieve the goals of the *Triple Aim* for older adults who are prescribed with antidepressants in their office-based outpatient visits.

Second, continuous quality improvement (CQI)[33] and other quality of care improvement programs in office-based outpatient care often focus on (1) improving

patient satisfaction with visits; (2) improving continuity of care among providers; and (3) other quality of care indicators (e.g., improving delivery of medical practice) by identifying and reducing unnecessary, avoidable procedures.[34] By understanding and using the national trend of potentially inappropriate antidepressant prescriptions as a benchmark, health care providers can bring clinical efforts on quality assurance and performance improvement in their practice related to antidepressant use among older adults in office-based outpatient visits.

Despite the importance of understanding the national trends of overall and potentially inappropriate antidepressant prescriptions descriptively, existing studies have several limitations. For example, previous studies[5,35] focused on the individual level rather than at the level of office-based outpatient visit; while they are informative understanding individual factors, they rarely convey information about physician- and/or practice-related factors. Other studies systematically excluded the older adult population,[36] were conducted outside the U.S.,[37] or are outdated.[37] In light of updated 2012 Beers Criteria and potential demographic shifts (i.e., aging America), an updated descriptive study of national trends for overall and potentially inappropriate antidepressant prescriptions among older adults in their office-based outpatient visits is needed.

1.4. Impact of Recent Policy Recommendation on Potentially Inappropriate Antidepressant Prescriptions

Despite the high prevalence (15-20%) of depression in older adults, depression and other related mood disorders (e.g., dysthymia) are often under-diagnosed and under-

treated.[9] While adults with depression are not likely to make psychiatry-related visits, they still seek care in general or other specialty visits, making "these visits particularly important opportunities to detect and initiate treatment of depression"[38(p. 279)] In light of providing care for depression in primary care and other specialty visits, screening for depression has become a "prominent component of the "detect—treat—improve" paradigm for undetected depression" since the mid-1990s.[38 (p.280)]

To provide systematic, comprehensive evidence for effectiveness and recommendations regarding depression screening, the U.S. Preventive Services Task Force (USPSTF) created a task force group on screening for depression in adults in late 1990s. The USPSTF is "an independent group of national experts in prevention and evidence-based medicine that works to improve the health of all Americans by making evidence-based recommendations about clinical preventive services such as screenings, counseling services, or preventive medications."[39] The USPSTF is supported by the Agency for Healthcare Research and Quality (AHRQ), as part of the U.S. Department of Health and Human Services. Currently, there are more than 40 standardized recommended practice guidelines (e.g., depression screening in adults and mammography for women) disseminated by the USPSTF.

In 2009, the USPSTF disseminated its practice recommendation that depression screening should be provided in eligible older adults ages 65 and over to "ensure accurate diagnosis, effective treatment and appropriate follow-up" related to depression and other mental health conditions. [40,41] While there are validated depression screening instruments (e.g., Geriatric Depression Scale (GDS) and Patient Health Questionnaire 9 (PHQ-9)), the USPSTF does not specify which depression screening instruments should be used.[40]

In existing literature, there are several studies that assess the policy impacts of recent USPSTF guidelines (e.g., mammography use[42] and pediatric urinalysis[43]). However, no study has yet assessed the impact of the 2009 depression screening recommendation. It is of question if the 2009 depression screening recommendation had a differential impact on diagnosing depression and other mental health conditions, as well as prescribing overall and potentially inappropriate antidepressants. Findings can help determine if the 2009 USPSTF depression screening recommendation has been beneficial in detecting and treating older adults with depression and other related mood disorders during their office-based outpatient visits. Findings may also suggest that future research may be needed to assess spill-over effects and their magnitudes of the 2009 USPSTF depression screening recommendation regarding the aforementioned outcomes as well as other important outcomes, such as patient-reported outcomes (e.g., health-related quality of life).

1.5. Depression Screening and Potentially Inappropriate Antidepressant Prescriptions in Clinical Practice

While depression screening is recommended by the USPSTF and other interest groups, such as the American College of Preventive Medicine (ACPM)[44] and American Heart Association (AHA),[45] there is a consistent controversy about the use of depression screening in clinical practice. Most randomized controlled trial (RCT) studies found no association between depression screening and patient outcomes (e.g., depressive symptoms).[46,47] When considering detection and treatment for depression and other related mental health conditions as intermediate outcomes, the role of depression

screening is still mixed in RCTs.[48] Based solely on findings from such RCTs, the Canadian Task Force on Preventive Health Care (CTFPHC)—the Canadian version of USPSTF—is opposed to recommend depression screening in clinical practice in Canada.[49]

However, these RCT studies employed relatively homogeneous, small study samples and systematically excluded older adults. Furthermore, as one study suggests, findings from depression-related RCTs are not representative of usual medical settings.[50] Thus, generalizability is questionable. Because of limited external validity from RCTs, greater external validity is needed using population-based observational studies. To my knowledge, there is only one population-based observational study,[51] which provides a promising evidence that depression screening may improve appropriate antidepressant use in office-based outpatient visits. The same study, however, only used overall antidepressant prescriptions as an outcome among the general population, and did not consider potentially inappropriate prescriptions among older adults.

A deeper understanding of the relationship between depression screening and potentially inappropriate antidepressant prescriptions is needed among older adults in their office-based outpatient visits. Findings may inform whether depression screening is consistent with the USPSTF recommendation and should be implemented in clinical practice for this specific elderly population group in the U.S.

1.6. Specific Aims

To address current gaps in research, the goals of proposed study are: (1) to explore patterns of overall and potentially inappropriate antidepressant prescriptions; (2)

to examine a policy impact of depression screening on (i) diagnosing depression and other mental health conditions and (ii) prescribing overall and potentially inappropriate antidepressant prescriptions; and (3) to determine the effect of depression screening in clinical practice among older adults in office-based outpatient settings. Using National Ambulatory Medical Care Survey (NAMCS) data from 2002 to 2012, which nationally represent office-based outpatient visits of all ages, the proposed dissertation project has the three following specific aims:

Aim #1: To describe prevalence rates (%) of (1) overall antidepressant prescriptions and (2) potentially inappropriate antidepressant prescriptions, and to understand factors associated with them among older adults ages 65 and over in office-based outpatient visits.

1.1. Overall antidepressant prescriptions

1.1.1. What is the prevalence of office-based outpatient visits that had any antidepressant prescription among older adults ages 65 and over in their office-base outpatient visits by year from 2002-2012?

1.1.2. What is the distribution of socio-demographic and health-related characteristics by the status of any antidepressant prescription among older adults ages 65 and over in their office-base outpatient visits by year from 2002 to 2012?

1.1.3. Which socio-demographic and health-related characteristics are associated with office-based outpatient visits that had any antidepressant prescription

among older adults ages 65 and over in their office-base outpatient visits by year from 2002 to 2012?

1.2. Potentially inappropriate antidepressant prescriptions using Beers Criteria

1.2.1. Using Beers Criteria, what is the prevalence of office-based outpatient visits that had potentially inappropriate antidepressant prescriptions among older adults ages 65 and over in their office-base outpatient visits by year from 2002 to 2012?

1.2.2. Using Beers Criteria, what is the distribution of socio-demographic and health-related characteristics by the status of potentially inappropriate antidepressant prescriptions among older adults ages 65 and over in their office-base outpatient visits by year from 2002 to 2012?

1.2.3. Using Beers Criteria, which socio-demographic and health-related characteristics are associated with office-based outpatient visits that had potentially inappropriate antidepressant prescriptions among older adults ages 65 and over in their office-base outpatient visits by year from 2002 to 2012?

For aim #1.2, Beers Criteria will be operationalized using: (1) the 2002 version; (2) the 2012 version; Operational definitions and rationale will be further described in the methods section.

Aim #2: To examine the policy impact of the 2009 U.S. Preventive Services Task Force (USPSTF) depression screening recommendation on (1) the diagnosis of depression; (2) the diagnosis of mental health conditions other than depression; and (3) overall antidepressant prescriptions; and (4) potentially inappropriate antidepressant

prescriptions between pre- (2006-2008) and post- (2010-2012) periods among older adults ages 65 and over in office-based outpatient visits.

2.1. Diagnosis of depression

2.1.1. Did the rate of diagnosis of depression increase by depression screening status after implementation of the 2009 USPSTF depression screening recommendation among older adults ages 65 and over in office-based outpatient visits?

2.1.2. Was there a differential impact of the 2009 USPSTF depression screening recommendation on the diagnosis of depression by depression screening status among older adults ages 65 and over in office-based outpatient visits?

2.2. Diagnosis of mental health conditions other than depression

2.2.1. Did the rate of diagnosis of mental health conditions other than depression increase by depression screening status after implementation of the 2009 USPSTF depression screening recommendation among older adults ages 65 and over in office-based outpatient visits?

2.2.2. Was there a differential impact of the 2009 USPSTF depression screening recommendation on the diagnosis of mental health conditions other than depression by depression screening status among older adults ages 65 and over in office-based outpatient visits?

2.3. Overall antidepressant prescriptions

2.3.1. Did the prevalence (%) of overall antidepressant prescriptions increase by depression screening status after implementation of the 2009 USPSTF

depression screening recommendation among older adults ages 65 and over in office-based outpatient visits?

2.3.2. Was there a differential impact of the 2009 USPSTF depression screening recommendation on the prevalence (%) of overall antidepressant prescriptions by depression screening status among older adults ages 65 and over in office-based outpatient visits?

2.4. Potentially inappropriate antidepressant prescriptions using Beers Criteria

2.4.1. Did the prevalence (%) of potentially inappropriate antidepressant prescriptions increase by depression screening status after implementation of the 2009 USPSTF depression screening recommendation among older adults ages 65 and over in office-based outpatient visits?

2.4.2. Was there a differential impact of the 2009 USPSTF depression screening recommendation on the prevalence (%) of potentially inappropriate antidepressant prescriptions by depression screening status among older adults ages 65 and over in office-based outpatient visits?

In aim #2.4, the version(s) of Beers Criteria will be considered based on findings from aim #1.2.

Aim #3: To explore a potential effect of depression screening on (1) the diagnosis of depression; (2) the diagnosis of mental health conditions other than depression; (3) overall antidepressant prescriptions; and (4) potentially inappropriate antidepressant prescriptions in the post-period (2010-2012) of the 2009 USPSTF depression screening recommendation among older adults ages 65 and over in office-based outpatient visits.

3.1. Diagnosis of depression

3.1.1. Does depression screening have an effect on the diagnosis of depression among older adults ages 65 and over in office-based outpatient visits?

3.2. Diagnosis of mental health conditions other than depression

3.2.1. Does depression screening have an effect on the diagnosis of mental health conditions other than depression among older adults ages 65 and over in office-based outpatient visits?

3.3. Overall antidepressant prescriptions

3.3.1. Does depression screening have an effect on the overall antidepressant prescriptions among older adults ages 65 and over in office-based outpatient visits?

3.4. Potentially inappropriate antidepressant prescriptions using Beers Criteria

3.4.1. Does depression screening have an effect on the potentially inappropriate antidepressant prescriptions among older adults ages 65 and over in office-based outpatient visits?

In order to address these aims, data from the NAMCS will be used. The NAMCS data present a unique opportunity to explore issues surrounding overall and potentially inappropriate antidepressant prescriptions among a nationally-representative sample of U.S. older adults in office-based outpatient settings. Overall, the proposed study has the following expected outcomes: First, I will estimate the prevalence (%) of overall and potentially inappropriate antidepressant prescriptions by year, and factors associated with them from 2002 to 2012. The findings will provide a deeper understanding of factors

driving the national trend of antidepressant-related prescribing patterns. Second, I will investigate whether a recent policy recommendation (i.e., depression screening) had any impact on (1) diagnosing mental health conditions, including depression, and (2) prescribing overall and potentially inappropriate antidepressants in older adults during their office-based outpatient visits. The findings will provide insights whether the policy recommendation has been beneficial for older adults who are often under-diagnosed and under-treated with depression and other related mood disorders. Third, I will determine whether depression screening—unlike findings from previous RCTs—should be provided to older adults in their office-based outpatient visits. Ultimately, this research project will bring positive impact by promoting clinical and policy efforts to improve patient safety in older adults who are prescribed with antidepressants in office-based outpatient settings.

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CHAPTER 2

Study Designs and Data Collection

2.1. Data Source and Study Population

I used data from the 2002-2012 National Ambulatory Medical Care Survey (NAMCS), which is administrated by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC).[1] The NAMCS is an annual, cross-sectional survey of visits to office-based physicians in outpatient settings. The NAMCS represents office-based outpatient care and provides reliable information about the provision and/or use of ambulatory medical care services in the United States.[1]

Using a multi-stage probability sampling design, data were collected from office-based physicians. First, a probability sample of primary sampling units (PSUs) was drawn. A PSU consists of "a county, a group of counties, county equivalents (such as parishes and independent cities), towns, townships, minor civil divisions (for some PSUs in New England), or a metropolitan statistical area (MSA)."[2(p. 9)] In the second stage, a probability of sample of practicing physicians within chosen PSUs was drawn. These physicians are further stratified by specialty groups (e.g., general and family practice, and psychiatry) within each PSU. Finally, each physician was randomly selected to a 1-week reporting period; during this period, data for a systematic random sample of patient visits to the physician were abstracted. Data include patients' socio-demographic characteristics

(e.g., age, sex, and race/ethnicity) and health-related information (e.g., comorbidity), as well as physician's diagnoses, procedures and medications provided.

The survey response rate varies from 58.3 to 70.4% (see Table 2.1) over the years. Of 90,472 visits (unweighted) for adults ages 65 and over in 2002-2012, I excluded observations with missing covariates (4.96%), leaving the final sample size of 85,987 visits (unweighted) (see Table 2.1). Further details of the survey, including descriptions, questionnaires, sampling methodology and datasets, are publicly available on the NAMCS website.[3]

Table 2.1. Study sample of office-based outpatient visits for adults ages 65 and older by year, NAMCS 2002-2012.

Year	Survey response rate	Study sample	
		Unweighted sample	Weighted visit
2002	70.4%	7,451	224,380,087
2003	66.9%	6,886	227,520,460
2004	64.7%	7,086	233,991,068
2005	61.5%	6,876	247,683,250
2006	58.9%	7,451	229,837,453
2007	61.6%	8,968	258,214,352
2008	59.1%	7,211	256,135,092
2009	62.1%	8,673	279,513,535
2010	58.3%	8,156	258,976,010
2011	-[a)]	8,247	255,736,330
2012	-[a)]	21,714	247,633,504
Total	58.3-70.4% (range)	98,719	247,238,286

Note: a) indicates that data are not available.

2.2. Key Measures

Antidepressant use:

- *Overall antidepressant prescriptions.* Using the *2015 American Hospital Formulary Service (AHFS) Compendium*,[4] Wolters Kluwer's *Drug Facts and Comparisons*,[5] and previous studies,[6-11] I identified prescribed antidepressant

medications using generic names (see Table 2.2). In 2002, up to six medications were recorded in each visit. From 2003-2010, up to eight medications were recorded in each visit, and the maximum number of medications recorded was increased to 12 in 2012. I included all antidepressant medications prescribed in the analytic sample to measure crude estimates. I created binary indicator variables for each generic name of antidepressants. For overall antidepressant prescriptions, I created a binary indicator (yes/no), aggregating the individual prescribed antidepressants.

- *Potentially inappropriate antidepressant prescriptions*. For potentially inappropriate antidepressant prescriptions, I constructed three different binary indicator variables (yes/no): (1) the 2012 version of Beers Criteria (see Table 2.2 for "independent of diagnosis" and Table 2.3 for "drug-disease or drug-syndrome interactions"); (2) the 2002 version of Beers Criteria (see Table 2.4 for details); and (3) the Beers Criteria contemporary to each year (i.e., the 2002 version for 2002-2011 and the 2012 version for 2012).[12,13]
    - 2012 version: I used the 2012 version to look at the national trends of potentially inappropriate antidepressant prescriptions *retrospectively*. Using the 2012 version, which contains clinically rigorous, up-to-date recommendations, would give a sense of how changes in the recent guideline may have been affected the prevalence (%) of potentially inappropriate antidepressant prescriptions by year from 2002 to 2012 among older adults ages 65 and over who had office-based outpatient visits.

- 2002 version: I also used the 2002 version in order to look at the national trends of potentially inappropriate antidepressant prescriptions *prospectively* since the earlier version of Beers Criteria was disseminated in 2002. Using the 2002 version, if the prevalence of potentially inappropriate antidepressant prescriptions decreased over time among antidepressant-related, office-based outpatient visits, it may be inferred that the Beers Criteria has been effectively used in clinical practice.
- Version contemporary to each year: Finally, the Beers Criteria contemporary to each year (i.e., the 2002 version for 2002-2011 and the 2012 version for 2012) were also used to further observe similarities or differences between 2002 and 2012 versions for potentially inappropriate antidepressant prescriptions.

Mental health conditions:

- *Mental health conditions*. In aim #1, mental health conditions are one of covariates. Using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM), I identified mental health diagnoses that are clinically relevant and have significant burden to older adults as follow: (1) depressive disorders; (2) bipolar disorders; (3) schizophrenia; (4) anxiety disorders; (5) personality disorders; (6) delirium, dementias and other cognitive impairment; and (7) others. Table 2.5 lists the ICD-9-CM diagnostic codes included in each category.[14]

- *Depression*. For aims #2.1.1, 2.1.2, and 3.1.1, diagnosis of depression is a dependent variable. I constructed a binary indicator variable (yes/no) using the ICD-9-CM diagnostic codes (296.2 & 296.3) (see Table 2.5).
- *Mental health conditions other than depression*. In aims #2.2.1, 2.2.2, and 3.2.1, diagnosis of mental health conditions other than depression is a dependent variable. Based on Table 2.5, I constructed a binary indicator variable (yes=any mental health condition diagnosed, except depression; no=otherwise).

Screening/counseling:

- *Depression screening*: In the "diagnostic and screening services section" of the NAMCS, depression screening is asked (yes/no) for the purpose of "early detection of health problems in asymptomatic individuals."[3] This binary variable, depression screening, is a key independent variable in aims #2 and 3.
- *Diet/nutrition education and counseling*: Under the "health education ordered or provided section" of the NAMCS, physicians were asked if diet/nutrition education and counseling were provided (yes/no) to the patient. This is a key instrumental variable in aim #3.
- *Exercise education and counseling*: Under the "health education ordered or provided section" of the NAMCS, physicians were asked if exercise education and counseling were provided (yes/no) to the patient. This is a key instrumental variable in aim #3.

Covariates:

Based on (1) previous studies,[6,9,10,15-28] (2) potential confounders related to research questions, and (3) availability in data, I selected a number of covariates to control for in the statistical analyses.

- *Socio-demographic characteristics*: These include: (1) age (65-74; 74-85; 85+); (2) gender (male and female); (3) race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and other); (4) region (Northeast, Midwest, South, and West); and (5) primary source of payment (Private, Medicare, Medicaid, and others).
- *Health-related, clinical characteristics*: These include: (1) reason for visit (acute/new problem, chronic problem, preventive care, pre-/post-surgery); (2) repeat of visits in the past 12 months; (3) physician specialty (primary care, psychiatry, and other specialties); (4) type of medical practice (solo/group practice vs. others); (5) metropolitan statistical area (MSA) status (yes/no); (6) provision of psychotherapy (yes/no); (7) time spent with doctor (minutes); (8) comorbid status (number of chronic conditions); and (9) polypharmacy (number of medications).

Operationalization of each variable is further described in Table 2.6. In addition, Table 2.6 summarizes which variables are to be included in each specific aim. They are also in accord with the analytical plans, which would be described below.

2.3. Analytical Plans

Aim #1: Aim #1 is a descriptive study and key statistical techniques include: univariate analysis (i.e., prevalence (%)), bivariate analysis (i.e., design-based *F*-statistics), and multivariate logistic regression analysis. A proposed analytical plan by each specific sub-aim in aim #1 is described below (see Table 2.7.1). Selected variables for each analytical plan are summarized in Table 2.6.

Table 2.7.1. Proposed analytical plan by specific aim #1

Aim #1	Proposed analytical plan
1.1.1.	• Calculate the prevalence (%) of overall antidepressant prescriptions as follows: # of office-based outpatient visits with any antidepressant prescribed / # of all office-based outpatient visits among older adults by each year.
1.1.2.	• Conduct a bivariate analysis (i.e., a two-way tabulation) on each of socio-demographic and health-related characteristics (see table 2.6) by the status of overall antidepressant prescriptions. Design-based *F*-statistics and *p*-value would be reported to observe significant, different patterns of each variable's distribution by the status of overall antidepressant prescriptions. It would be conducted by each year.
1.1.3.	• Conduct a multivariate logistic regression analysis of the status of overall antidepressant prescriptions on socio-demographic and health-related characteristics (see table 2.6). 95% confidence interval and *p*-value of each regressor would be reported to see its significant relationship with the overall antidepressant prescriptions, holding other variables constant.
1.2.1.	• Calculate the prevalence (%) of potentially inappropriate antidepressant prescriptions as follows: # of office-based outpatient visits with potentially inappropriate antidepressant prescribed / # of all office-based outpatient visits among older adults by each year.
1.2.2.	• Conduct a bivariate analysis (i.e., a two-way tabulation) on each of socio-demographic and health-related characteristics (see table 2.6) by the status of potentially inappropriate antidepressant prescriptions. Design-based *F*-statistics and *p*-value would be reported to observe significant, different patterns of each variable's distribution by the status of potentially inappropriate antidepressant prescriptions. It would be conducted by each year.
1.2.3.	• Conduct a multivariate logistic regression analysis of the status of potentially inappropriate antidepressant prescriptions on socio-demographic and health-related characteristics (see table 2.6). 95% confidence interval and *p*-value of each regressor would be reported to

Aim #1	Proposed analytical plan
	see its significant relationship with the potentially inappropriate antidepressant prescriptions, holding other variables constant.

Aim #2: Aim #2 focuses on policy evaluation and difference-in-differences (DID) approach is the key statistical technique to be used. The DID method is appropriate, as it compares treatment (i.e., those who received depression screening) and control (i.e., those who did not receive depression screening) groups in terms of outcome changes (e.g., overall antidepressant prescriptions) over time (i.e., pre-/post-intervention).[29] The key assumption when applying the DID method is that unobserved selection bias—or unobserved heterogeneity—in participation (i.e., depression screening) may present, but is time-invariant.[29] Then, such unobserved selection bias can be canceled out by using the DID method, and the impact of 2009 USPSTF depression screening recommendation can be measured. A proposed analytical plan by each specific sub-aim in aim #2 is described below (see Table 2.7.2). Selected variables for each analytical plan are summarized in Table 2.6.

Table 2.7.2. Proposed analytical plan by specific aim #2

Aim #2	Proposed analytical plan
2.1.1.	• Calculate the prevalence (%) of depression diagnosed by (1) depression screening status and (2) by pre- (2006-2008) and post- (2010-2012) periods. • Descriptively observe the patterns using bivariate analyses (i.e., a two-way tabulation) of these key variables. Design-based *F*-statistics and *p*-value would be reported for each pattern.
2.1.2.	• Conduct a multivariate logistic regression analysis of the depression diagnosed on depression screening status, time indicator (pre/post), and the interaction of depression screening status and time indicator, while controlling for all other socio-demographic and health-related characteristics (see table 2.6). The *t*-statistic and *p*-value of the interaction term would be reported to determine a differential impact of the 2009 USPSTF depression screening recommendation on the diagnosis of depression.

Aim #2	Proposed analytical plan
2.2.1.	• Calculate the prevalence (%) of other mental health conditions, excluding depression, diagnosed by (1) depression screening status and (2) by pre- (2006-2008) and post- (2010-2012) periods. • Descriptively observe the patterns using bivariate analyses (i.e., a two-way tabulation) of these key variables. Design-based *F*-statistics and *p*-value would be reported for each pattern.
2.2.2.	• Conduct a multivariate logistic regression analysis of the mental health conditions diagnosed (except depression) on depression screening status, time indicator (pre/post), and the interaction of depression screening status and time indicator, while controlling for all other socio-demographic and health-related characteristics (see table 2.6). The *t*-statistic and *p*-value of the interaction term would be reported to determine a differential impact of the 2009 USPSTF depression screening recommendation on the diagnosis of mental health conditions other than depression.
2.3.1.	• Calculate the prevalence (%) of overall antidepressant prescriptions by (1) depression screening status and (2) by pre- (2006-2008) and post- (2010-2012) periods. • Descriptively observe the patterns using bivariate analyses (i.e., a two-way tabulation) of these key variables. Design-based *F*-statistics and *p*-value would be reported for each pattern.
2.3.2.	• Conduct a multivariate logistic regression analysis of the overall antidepressant prescriptions on depression screening status, time indicator (pre/post), and the interaction of depression screening status and time indicator, while controlling for all other socio-demographic and health-related characteristics (see table 2.6). The *t*-statistic and *p*-value of the interaction term would be reported to determine a differential impact of the 2009 USPSTF depression screening recommendation on the overall antidepressant prescriptions.
2.4.1.	• Calculate the prevalence (%) of potentially inappropriate antidepressant prescriptions by (1) depression screening status and (2) by pre- (2006-2008) and post- (2010-2012) periods. • Descriptively observe the patterns using bivariate analyses (i.e., a two-way tabulation) of these key variables. Design-based *F*-statistics and *p*-value would be reported for each pattern.
2.4.2.	• Conduct a multivariate logistic regression analysis of the potentially inappropriate antidepressant prescriptions on depression screening status, time indicator (pre/post), and the interaction of depression screening status and time indicator, while controlling for all other socio-demographic and health-related characteristics (see table 2.6). The *t*-statistic and *p*-value of the interaction term would be reported to determine a differential impact of the 2009 USPSTF depression screening recommendation on the overall antidepressant prescriptions.

Aim #3: Aim #3 focuses on the effect of depression screening on four different outcomes—(1) the diagnosis of depression; (2) the diagnosis of mental health conditions other than depression; (3) overall antidepressant prescriptions; and (4) potentially inappropriate antidepressant prescriptions—in clinical practice. To determine such effect, however, selection bias of physicians (e.g., physicians selectively choose whom to give depression screening) is a serious methodological concern.[26] To address such concern, an instrumental variable (IV) analysis is proposed in this aim #3, and at least two instrumental variables would be selected: (1) diet/nutrition education and counseling, and (2) exercise education and counseling. The rationale for selecting these IVs are explained in Mojtabai's work (i.e., they are likely correlated with depression screening and are not likely associated with the outcomes).[26] A proposed analytical plan by each specific sub-aim in aim #3 is described below (see Table 2.7.3). Selected variables for each analytical plan are summarized in Table 2.6.

Table 2.7.3. Proposed analytical plan by specific aim #3

Aim #3	Proposed analytical plan
3.1.1.	• Check the assumption of instrumental variables (diet/nutrition and exercise counseling) are highly correlated with the key independent variable, depression screening, and have a low correlation with the key dependent variable, diagnosis of depression. • When the assumption is met, conduct a two-stage least squares (2SLS) multivariate regression analysis: that is, (1) regress depression screening on instrumental variables; then, (2) regress diagnosis of depression on the stored information from (1), while controlling for all other socio-demographic and health-related characteristics (see table 2.6). • Check the regression model for (1) endogeneity and (2) over-identification issues using a Hausman specification test, provided as a post-estimation technique in Stata.[30] • Report the full model with coefficients, 95% CIs, and *p*-values to discuss the role of depression screening on the diagnosis of depression.
3.2.1.	• Check the assumption of instrumental variables (diet/nutrition and exercise counseling) are highly correlated with the key independent variable, depression screening, and have a low correlation with the key

Aim #3	Proposed analytical plan
	dependent variable, diagnosis of mental health conditions other than depression. • When the assumption is met, conduct a two-stage least squares (2SLS) multivariate regression analysis: that is, (1) regress depression screening on instrumental variables; then, (2) regress diagnosis of mental health conditions other than depression on the stored information from (1), while controlling for all other socio-demographic and health-related characteristics (see table 2.6). • Check the regression model for (1) endogeneity and (2) over-identification issues using a Hausman specification test, provided as a post-estimation technique in Stata.[30] • Report the full model with coefficients, 95% CIs, and *p*-values to discuss the role of depression screening on the diagnosis of mental health conditions other than depression.
3.3.1.	• Check the assumption of instrumental variables (diet/nutrition and exercise counseling) are highly correlated with the key independent variable, depression screening, and have a low correlation with the key dependent variable, overall antidepressant prescriptions. • When the assumption is met, conduct a two-stage least squares (2SLS) multivariate regression analysis: that is, (1) regress depression screening on instrumental variables; then, (2) regress overall antidepressant prescriptions on the stored information from (1), while controlling for all other socio-demographic and health-related characteristics (see table 2.6). • Check the regression model for (1) endogeneity and (2) over-identification issues using a Hausman specification test, provided as a post-estimation technique in Stata.[30] • Report the full model with coefficients, 95% CIs, and *p*-values to discuss the role of depression screening on the overall antidepressant prescriptions.
3.4.1.	• Check the assumption of instrumental variables (diet/nutrition and exercise counseling) are highly correlated with the key independent variable, depression screening, and have a low correlation with the key dependent variable, potentially inappropriate antidepressant prescriptions. • When the assumption is met, conduct a two-stage least squares (2SLS) multivariate regression analysis: that is, (1) regress depression screening on instrumental variables; then, (2) regress potentially inappropriate antidepressant prescriptions on the stored information from (1), while controlling for all other socio-demographic and health-related characteristics (see table 2.6). • Check the regression model for (1) endogeneity and (2) over-identification issues using a Hausman specification test, provided as a post-estimation technique in Stata.[30]

Aim #3	Proposed analytical plan
	• Report the full model with coefficients, 95% CIs, and *p*-values to discuss the role of depression screening on the potentially inappropriate antidepressant prescriptions.

In each aim, I would use Stata 13.1[31] for all statistical analyses and would employ the ***svy*** commands in Stata to account for the complex sample design (i.e., unequal probability of selection, clustering and stratification) as well as pooling multiple year datasets from the NAMCS.

2.4. Potential challenges, limitations, and solutions

The proposed study is not free from potential challenges and limitations. First, the NAMCS does not collect injury-related ICD-9-CM diagnostic codes (e.g., EXXX.XX) since 2005. For consistency, I did not include one of the conditions when defining the potentially inappropriate use of antidepressants—interaction between history of falls or fractures (E880-E888) and TCAs/SSRIs (see Table 2.3). It must be clearly acknowledged. Second, a number of patient-related omitted variables (e.g., marital status, nativity status, income and educational attainment) should be acknowledged, as they can potentially confound my results. Fourth, in aim #3, while the selection of instrumental variables was grounded on a previous study,[26] they may not be ideal or may still have some endogeneity problems in my study. In such case, I may need to approach the research questions differently—using structural equation modeling, for example. As a scientific researcher, I would further acknowledge other potential challenges and limitations and try to address them clearly throughout my study.

Table 2.2. Antidepressant medications by class[4]

Tricyclics (TCAs)
- Amitriptyline[a), b), f)]
- Amoxapine[b)]
- Clomipramine[a), b), f)]
- Desipramine[b)]
- Doxepin[a), b), f)]
- Imipramine[a), b), f)]
- Maprotiline
- Nortriptyline[b)]
- Protriptyline[b)]
- Trimipramine[a), b), f)]

Serotonin Modulators
- Nefazodone
- Trazodone
- Vilazodone[e)]
- Vortioxetine[e)]

Selective Serotonin Reuptake Inhibitors (SSRIs)
- Citalopram
- Escitalopram
- Fluoxetine
- Fluvoxamine
- Paroxetine[b)]
- Sertraline

Monoamine Oxidase Inhibitors (MAOIs)
- Isocarboxazid
- Phenelzine
- Tranylcypromine
- Rasagiline[c)]
- Selegiline[c)]

Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)
- Desvenlafaxine
- Duloxetine
- Levomilnacipran[e)]
- Venlafaxine
- Milnacipran[d)]

Miscellaneous
- Bupropion
- Mirtazapine

Note: a) denotes tertiary TCAs; b) denotes drugs with strong anticholinergic properties; c) denotes a MAO-B inhibitor and is primarily classified as anti-Parkinsonian agents; d) is primarily classified as fibromyalgia agents; e) indicates that it is not available in NAMCS; and f) indicates that it should be avoided, regardless of diagnosis, according to 2012 Beers criteria.

Table 2.3. 2012 Beers criteria for potentially inappropriate antidepressant use in older adults due to drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome[12]

Disease or syndrome (ICD-9-CM code)	Antidepressant[a)]	Rationale	Recommendation	Quality of Evidence	Strength of recommendation
Cardiovascular					
Syncope (780.2, 992.1)	Tertiary TCAs	Increase risk of orthostatic hypotension or bradycardia	Avoid	Moderate	Strong
Central nervous system					
Chronic seizures or epilepsy (345, 780.33)	bupropion; maprotiline	Lowers seizure threshold; may be acceptable in patients with well-controlled seizures in whom alternative agents have not been effective	Avoid	Moderate	Strong
Delirium (290.11, 290.3, 290.41, 291.0, 292.81, 293.0, 293.1)	TCAs; Anticholinergics	Induce or worsen delirium in older adults; if discontinuing drugs used chronically, taper to avoid withdrawal symptoms	Avoid	Moderate	Strong
Dementia and cognitive impairment (290, 291.2, 292.82, 294.10, 294.11, 294.20, 294.21, 331.0, 331.19, 331.82, 331.83)	Anticholinergics	Avoid because of adverse CNS effects	Avoid	High	Strong
History of falls or fractures (E880-E888)[b)]	TCAs; SSRIs	Ability to produce ataxia, impaired psychomotor function, syncope, and additional falls	Avoid unless safer alternatives are not available	High	Strong
Gastrointestinal					
Chronic constipation (564)	Tertiary TCAs; Anticholinergics	Can worsen constipation	Avoid unless no other alternatives	Moderate to low	Weak
Lower urinary tract symptoms, benign prostatic hyperplasia (600)	Anticholinergics	May decrease urinary flow and cause urinary retention	Avoid in men	Moderate	Inhaled agents: strong; others: weak

Note: a) refers to appendix 1 for full description; and b) excluded in the analysis for consistency, as NAMCS only collected external cause information using ICD-9-CM in 2002-2004.

Table 2.4. 2002 Beers criteria for potentially inappropriate antidepressant use in older adults, based on 2012 Beers criteria.[12,13]

Medications moved to another category or modified since 2002	
Independent of diagnoses or conditions	• None
Considering diagnoses	• Fluoxetine, citalopram, fluvoxamine, paroxetine, and sertraline with syndrome of inappropriate antidiuretic hormone secretion
Medications removed since 2002	
Independent of diagnoses or conditions	• Daily fluoxetine
Considering diagnoses	• Fluoxetine with anorexia and malnutrition • Monoamine oxidase inhibitors (MAOIs) with insomnia

Table 2.5. Mental health diagnosis[14]

Diagnosis	ICD-9-CM diagnostic code (290-319)
Affective disorder	
Major depression	296.2 & 296.3
Dysthymia	300.4
Other affective disorder	296.1, 296.81, 296.82, 296.9, & 311.0
Bipolar disorder	
Bipolar disorder	296.00-296.06, 296.40-296.46, 296.50-296.56, 296.60-296.66, 296.7, 296.80, 296.89
Schizophrenia	
Schizophrenia	295
Delirium, dementia, and other cognitive impairment	
Delirium	290.11, 290.3, 290.41, 291.0, 292.81, 293.0, 293.1
Dementia and other cognitive impairment	290, 291.2, 292.82, 294.10, 294.11, 294.20, 294.21, 331.0, 331.19, 331.82, 331.83
Anxiety Disorders	
Generalized anxiety disorder (GAD)	300.02
Panic disorder with or without agoraphobia	300.01 & 300.21
Obsessive-compulsive disorder	300.3
Personality Disorders	
Personality disorders	301
Others	Otherwise

Table 2.6. Key variables by specific aim.

Variable	Operationalization	Specific aim																	
		Aim #1						Aim #2								Aim #3			
		1.1.1.	1.1.2.	1.1.3.	1.2.1.	1.2.2.	1.2.3.	2.1.1.	2.1.2.	2.2.1.	2.2.2.	2.3.1.	2.3.2.	2.4.1.	2.4.2.	3.1.1.	3.2.1.	3.3.1.	3.4.1.
Year																			
2002-2004		X	X	X	X	X	X												
2005		X	X	X	X	X	X												
2006-2008		X	X	X	X	X	X	X	X	X	X	X	X	X	X				
2009		X	X	X	X	X	X												
2010-2012		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Antidepressant use																			
Overall antidepressant prescriptions	1=yes; 0=no	D V	D V	D V								D V	D V					D V	
Potentially inappropriate antidepressant prescriptions (2002 version)	1=yes; 0=no				D V	D V	D V							D V	D V				D V
Potentially inappropriate antidepressant prescriptions (2012 version)	1=yes; 0=no				D V	D V	D V							D V	D V				D V
Potentially inappropriate antidepressant prescriptions (2002 version for 2002-2011 and 2012 version for 2012)	1=yes; 0=no				D V	D V	D V							D V	D V				D V
Mental health conditions																			
Mental health	1=major depression; 2=dysthymia; 3=other affective disorders; 4=bipolar disorders; 5=schizophrenia; 6=delirium, dementia and other cognitive deficits; 7=anxiety-related disorders;		C	C		C	C												

	8=personality disorders; 9=others																		
Depression	1=major depression; 0=otherwise					D V	D V								D V				
Mental health conditions other than depression	1= 2 to 9 in mental health; 0=otherwise							D V	D V							D V			
Screening/counseling																			
Depression screening	1=yes; 0=no					IV	IV	IV	IV	IV	IV	IV	IV	IV	IV	IV	IV	IV	IV
Diet/nutrition education and counseling	1=yes; 0=no														Inst V	Inst V	Inst V	Inst V	
Exercise education and counseling	1=yes; 0=no														Inst V	Inst V	Inst V	Inst V	
Socio-demographic characteristics																			
Age	1=65-74; 2=75-84; 3=85+	C	C	C	C		C		C		C		C	C	C	C	C	C	C
Gender	1=male; 2=female	C	C	C	C		C		C		C		C	C	C	C	C	C	C
Race/ethnicity	1=non-Hispanic white; 2=non-Hispanic black; 3=Hispanic; 4=others	C	C	C	C		C		C		C		C	C	C	C	C	C	C
Region	1=Northeast; 2=Midwest; 3=South; 4=West	C	C	C	C		C		C		C		C	C	C	C	C	C	C
Primary source of payment	1=private; 2=Medicare; 3=Medicaid; 4=others	C	C	C	C		C		C		C		C	C	C	C	C	C	C
Health-related, clinical characteristics																			
Reason for visit	1=acute problem; 2=routine chronic problem; 3=pre-/post-surgery; 4=preventive care	C	C	C	C		C		C		C		C	C	C	C	C	C	C
Repeat of visits in the past 12 months	0=none; 1=1-2 visits; 2=3-5 visits; 3=6+ visits	C	C	C	C		C		C		C		C	C	C	C	C	C	C
Physician specialty	1=primary care; 2=psychiatry; 3=others	C	C	C	C		C		C		C		C	C	C	C	C	C	C
Type of medical practice	1=solo/group practice; 2=others	C	C	C	C		C		C		C		C	C	C	C	C	C	C
Metropolitan statistical area (MSA)	1=yes; 0=no	C	C	C	C		C		C		C		C	C	C	C	C	C	C
Provision of psychotherapy	1=yes; 0=no	C	C	C	C		C		C		C		C	C	C	C	C	C	C

Time spent with doctor	1= < 15 min.; 2=15-20 min; 3=21-30 min; 4= > 30 min.	C	C	C	C	C	C	C	C	C	C	C	C
Multiple chronic conditions	0=none; 1=1; 2=2-3; 4=4+	C	C	C	C	C	C	C	C	C	C	C	C
Number of medications	1=0-2; 2=3-5; 3=6+	C	C	C	C	C	C	C	C	C	C	C	C

Note: X=included; DV=dependent variable; IV=independent variable; InstV=instrumental variable; and C=covariate.

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CHAPTER 3

Manuscript #1: Potentially Inappropriate Antidepressant Use among Older Adults in Office-based Outpatient Settings: National Trends from 2002 to 2012

Keywords: antidepressant, office-based care, older adults, Beers Criteria, inappropriate use, prescribing pattern

Abstract text word count: 98 (≤ 100)
Article text word count: 2,946 (≤ 3,000)
Number of tables: 3
Number of figures: 2
Number of appendices: 4

Joint Acknowledgment/Disclosure Statement*:* Dr. Rhee conceived the study, acquired data, analyzed and interpreted the data, led the writing of the manuscript, and oversaw every aspect of the study. Drs. Schommer, Capistrant, Hadsall, and Uden contributed to the interpretation of the data, and critically revised the manuscript.

Conference Presentation: This study was presented at the 21st Annual International Meeting of International Society of Pharmacoeconomics and Outcomes Research (ISPOR) on May 21-25, 2016 (Washington, DC), and listed as a finalist for the Best Research Podium Presentation Award.

Funding Source: As part of authors' regular salary and fringe benefits, different departments from the University of Minnesota provided financial support for this study. This funding arrangement ensured the authors' independence in writing and publishing this original research.

Conflict of Interest: The authors declare that they do not have a conflict of interest.

Disclaimers: Publicly available data were obtained from the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC). Analyses, interpretation, and conclusions are solely those of the authors and do not necessarily reflect the views of the Division of Health Interview Statistics or NCHS of the CDC.

Compliance with Ethical Standards: Using publicly available de-identified data, the research procedure for this study was exempted from the University of Minnesota Institutional Review Board.

ABSTRACT

Using data from the 2002-2012 National Ambulatory Medical Care Survey, we calculated that the prevalence of overall antidepressant prescriptions increased almost twofold from 5.2% in 2002 to 10.1% in 2012 among older adults in their office-based visits. Approximately one in 10 antidepressant-related visits (or 2.2 million visits annually) among older adults was exposed to the risk of potentially avoidable adverse drug events. Amitriptyline and doxepin were the two most frequent disease-independent potentially inappropriate antidepressants. Racial/ethnic minorities, and Medicaid beneficiaries were associated with higher odds of potentially inappropriate antidepressant prescriptions ($p<0.05$). Efforts to minimize potentially inappropriate antidepressant prescriptions are needed.

Word Count: 98 (out of 100)

3.1 Introduction

Antidepressant use increased nearly 400% between periods of 1988-1994 and 2005-2008 in all ages,[1] and antidepressants are now among the top three most prescribed medication classes in the U.S.,[2,3] accounting for more than 260 million prescriptions each year.[3] In addition, antidepressants were the ninth most costly medications during the period of 2007-2011 in the U.S., accounting for approximately $20 billion in sales in 2011.[4] Despite the increasing rate of antidepressant use in the general population lately, relatively little is known about the prevalence of and possible factors for potentially inappropriate use of antidepressants among adults ages 65 and older (hereafter referred to as older adults) in office-based outpatient settings.

Potentially inappropriate medications are not only continuously prescribed,[5-8] but also remain problematic as they are associated with potentially avoidable healthcare expenditures,[9-11] estimated to be $7.2 billion in a 2001-2002 study.[11] In particular, potentially inappropriate medications are associated with increased hospitalization,[12-16] morbidity,[17] and mortality rates[15] in older adults. Other studies, however, suggest mixed results (e.g., no association between potentially inappropriate antidepressant use and mortality).[18-21] Because avoiding, or reducing, potentially inappropriate use of any medication is an effective strategy to minimize adverse drug events and other medication errors,[5,6,22] the incidence and/or prevalence of potentially inappropriate medication use may be used as one of quality of care indicators.

For quality assurance and performance improvement in office-based outpatient settings, the estimates of overall and potentially inappropriate antidepressant use need to be updated regularly because the availability and indications of antidepressants continue

to evolve. Previous studies have several limitations. For example, previous studies[3,23,24] focused on the individual level rather than at the level of office-based outpatient visit; while they are informative understanding individual factors, they rarely convey information about physician- and/or practice-related factors. Other studies systematically excluded the older adult population,[25] were conducted outside the U.S.,[26] or are simply outdated as they used earlier versions of Beers Criteria reflecting earlier time periods.[26,27]

To fill in existing gaps in literature, we address the following research questions: What are the national prevalence rates of overall and potentially inappropriate antidepressant prescriptions among older adults in office-based outpatient visits? Which potentially inappropriate antidepressants are most commonly prescribed? Which demographic and clinical characteristics are associated with the odds of two outcomes, overall and potentially inappropriate antidepressant prescriptions, among older adults in office-based outpatient visits? In light of updated 2012/2015 Beers Criteria[5,6] and rapid population aging, we provide an updated descriptive study of U.S. trends for overall and potentially inappropriate antidepressant prescriptions among older adults in their office-based outpatient visits, which may be used as a benchmark for future changes in office-based outpatient care.

3.2 Methods

Data Source and Study Sample

We used 2002- 2012 National Ambulatory Medical Care Survey (NAMCS), administrated by National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC).[28] The NAMCS is an annual, cross-sectional survey of

visits to office-based physicians in outpatient settings. The NAMCS represents office-based outpatient care and provides reliable information about the provision and/or use of ambulatory medical care services in the United States.[28] To estimate the prevalence of overall and potentially inappropriate antidepressant prescriptions, we selected visits for adults ages 65 and over (n=98,719 unweighted) in our analytic sample. For consistency of variables across years and sample size issues, we only used the samples from 2009-2012 (n=46,790 unweighted) for descriptive and multivariate logistic regression analyses. We excluded observations with all missing covariates (6.9%), leaving the final sample size of 43,550. Using publicly available data, the research procedure for this study was exempted from the University of Minnesota Institutional Review Board. Further details of the survey, including descriptions, questionnaires, sampling methodology and datasets, are publicly available on the NAMCS website.[29]

Measures

Dependent variables. The NAMCS collects up to eight medications in 2002-2011 and up to 10 medications in 2012. Using the *2015 American Hospital Formulary Service* (AHFS) *Compendium*,[30] Wolters Kluwer's *Drug Facts and Comparisons*,[31] and previous studies,[23,26,27,32-34] we identified prescribed antidepressant medications using generic names (see Appendix 3.1). We constructed a binary variable (yes/no) for overall antidepressant prescriptions.

Beers and his colleagues developed an inventory of potentially inappropriate medications (hereafter referred to as Beers Criteria) for older adults living in nursing homes in 1991.[35] The Beers Criteria were updated over time[5,6,36,37] and are now

applicable to older adults in all settings of geriatric care.[5,6] For potentially inappropriate antidepressant prescriptions, we constructed a binary variable (yes/no) using the 2012/2015 Beers Criteria (see Appendices 3.1 and 3.2)[5] among those who had antidepressant-related office-based outpatient visits.

Control variables. Based on previous studies,[23,27,33,38-46] we identified a number of covariates. We included demographic variables: age (65-74, 75-84, or 85+), gender, race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, or others), region (Northeast, Midwest, South, or West), primary source of payment (Medicare, Medicaid, private, or others), reason for visit (acute problem, routine chronic problem, preventive care, or pre- or post-surgery care), and repeat of visits within the past 12 months (none, 1-2, 3-5, or 6+). We also included clinical characteristics as follow: physician specialty (primary care, psychiatry, or others), type of medical practice (solo or others), metropolitan statistical area (MSA) status (yes/no), mental health diagnoses (see Appendix 3.3),[47] psychotherapy provided (yes/no), time spent with doctor (<15, 15-20, 21-30, or >30 min.), number of chronic conditions (none, 1, 2-3, or 4+), and number of medications (0-2, 3-5, or 6+). The number of chronic conditions was based on 14 chronic conditions (yes/no) collected by the NAMCS (e.g., arthritis, congestive heart failure, and diabetes). The variable, repeat of visits, had the largest missing proportion (28.1%), and was imputed based on age, gender and the number of medications using the *hotdeck* imputation technique.[48] Other variables that had missing values included: primary source of payment (3.8%), reason for visit (1.4%), and the number of chronic conditions (2.3%). Observations with all of these missing values (6.9%) were systematically excluded.

Data Analysis

First, we examined the extent to which demographic and clinical characteristics differed in older adults by the antidepressant prescription status. We used cross-tabulations and design-based *F*-tests to investigate differences by the antidepressant prescription status. Second, we estimated prevalence rates of overall and potentially inappropriate antidepressant prescriptions by year. Then, we estimated the prevalence of potentially inappropriate antidepressant prescriptions by disease (or condition) status. Third, we ran multivariate logistic regression analyses to identify demographic and clinical factors associated with overall and potentially inappropriate antidepressant prescriptions, respectively. We included the year variable to adjust for fixed effects in the multivariate logistic regression models in order to correctly estimate the average odds of antidepressant prescriptions over the whole time period. We used Stata 13.1[49] for all analyses and we employed the *svy* commands in Stata to account for the complex sample design of the NAMCS (i.e., unequal probability of selection, clustering and stratification).

3.3 Results

Sample Characteristics

Table 3.1 presents demographic and clinical characteristics of visits among older adults by the antidepressant prescription status. Except age and region, all characteristics had statistically significant differences by the antidepressant prescription status. Older adults who made office-based outpatient visits were more likely to be ages under 75 (50.7%), female (56.8%), predominantly non-Hispanic White (80.7%), and had Medicare (81.1%) as a primary source of payment. In antidepressant-related office-based outpatient

visits, female older adults and older adults living in the South were more likely to have antidepressant prescriptions.

Furthermore, more than half of older adults had at least three office-based outpatient visits (57.6%), and their primary reason for visit was routine chronic problems (54.3%). Only 1.1% of all visits made by older adults had psychiatry as a primary physician specialty, and the majority of visits was solo (92.3%) as type of medical practice, and located in the MSA (87.3%). In addition, majority of older adults was not diagnosed with mental health disorders (94.7%) and did not receive psychotherapy (99.3%) at the time of data were collected. Finally, more than half of older adults saw their doctor less than or equal to 20 minutes (66.5%), had at least two multiple chronic conditions (60.2%), and had at least three medications prescribed (54.9%).

<Table 3.1 about here>

Prevalence of Antidepressant Prescriptions

Figure 3.1 presents the prevalence of overall and potentially inappropriate antidepressant prescriptions among older adults in office-based outpatient visits by year. The prevalence of overall antidepressant prescriptions increased almost twofold over time from 5.2% in 2002 to 10.1% in 2012 (see Appendix 3.4 for exact estimates). The prevalence of potentially inappropriate antidepressant prescriptions in given all office-based outpatient visits made by older adults, however, remains consistent around 1.0% across years (see Appendix 3.4 for exact estimates). In given antidepressant-related visits, the prevalence of potentially inappropriate antidepressant prescriptions decreases from 17.0% in 2002 to 10.1% in 2012 (see Figure 3.2).

<Figures 3.1 and 3.2 about here>

Potentially Inappropriate Antidepressant Prescriptions

Table 3.2 shows the prevalence of potentially inappropriate antidepressant prescriptions by disease (or condition) status in antidepressant-related visits from 2010 to 2012. Approximately 10.6% of visits with antidepressant prescriptions were identified to be potentially inappropriate. Of these visits, 97.2% were disease-independent (i.e., regardless of diseases or conditions) potentially inappropriate antidepressants, and 8.2% were disease-dependent (i.e., due to drug-disease or drug-syndrome interactions) potentially inappropriate antidepressants (mutually not exclusive). About 5.0% of visits with potentially inappropriate antidepressant prescriptions were both disease-independent and disease-dependent. Among disease-independent potentially inappropriate antidepressants, the most common antidepressants were amitriptyline (67.7%), doxepin (15.4%), imipramine (8.3%), and clomipramine (5.9%). For disease-dependent potentially inappropriate antidepressants, chronic constipation and tertiary tricyclics or anticholinergics (7.0%), and benign prostatic hyperplasia and anticholinergics (1.1%) were the two most common cases.

<Table 3.2 about here>

Odds of Antidepressant Prescriptions

Table 3.3 presents the results of two multivariate logistic regression models estimating the odds of two outcomes: overall and potentially inappropriate antidepressant prescriptions. When adjusted for other covariates, being ages 75-84 and 85+ had significantly lower odds of overall antidepressant prescriptions by 14.7% and 25.3% ($P<0.05$), respectively. When compared to non-Hispanic Whites, non-Hispanic Blacks, Hispanics and others had significantly lower odds of overall antidepressant prescriptions

by 56.0%, 23.4% and 53.2% (P<0.05), respectively. Older adults who made visits to psychiatry had 10.71 times higher odds of overall antidepressant prescriptions when compared to those with primary care visits (95% CI 5.67-20.21; P<0.001). When compared to those who were not diagnosed with any mental disorder, older adults with mental health diagnoses had 5.78 times higher odds of overall antidepressant prescriptions (95% CI 4.61-7.23; P<0.01). Compared to those with no medication prescribed, older adults with three to five medications had 8.03 times higher odds of overall antidepressant prescriptions (95% CI 6.29-10.25; P<0.001) and those with equal to or more than six medications had 23.35 times higher odds of overall antidepressant prescriptions (95% CI 18.87-28.90; P<0.001).

For potentially inappropriate antidepressant prescriptions as a key outcome of interest, racial/ethnic minority groups other than non-Hispanic Blacks and Hispanics were 3.61 times higher odds when compared to non-Hispanic Whites (95% CI 1.49-8.72; P<0.001). When compared to older adults with Medicare as a primary source of payment, those with Medicaid as a primary source of payment had 2.54 times higher odds of potentially inappropriate antidepressant prescriptions (95% CI 1.04-6.18; P<0.05). Older adults with six or more repeated visits had significantly lower odds of potentially inappropriate antidepressant prescriptions by 46% (P<0.05). While older adults, who had psychiatry as their primary visits, had 3.97 times the odds of potentially inappropriate antidepressant prescriptions (95% CI 1.53-10.33; P<0.05), older adults with mental health diagnoses had lower odds of potentially inappropriate antidepressant prescriptions by 83.1% (P<0.001). Unlike the case in the overall antidepressant prescriptions, the time trend was associated with the odds of potentially inappropriate antidepressant

prescriptions. For instance, when compared to the year 2009, subsequent following years were almost twice higher odds of potentially inappropriate antidepressant prescriptions (P<0.05), when controlling for other covariates.

<Table 3.3 about here>

3.4 Discussion

This is the first study to use nationally representative data for estimating the prevalence rates of overall and potentially inappropriate antidepressant prescriptions, and factors associated with these outcomes among older adults in their office-based outpatient visits using the 2012/2015 Beers Criteria. First, one of major findings was that the overall antidepressant prescriptions in given all office-based outpatient visits made by older adults increased nearly twofold from 5.2% in 2002 to 10.1% in 2012. This is similar to previous studies conducted in different settings in the U.S.[50-52] Descriptively speaking, the finding suggests that the majority of antidepressant prescriptions was provided without psychiatric diagnoses or by non-psychiatrist providers, and this is consistent with a previous study.[52] Estimates in this study, however, are a bit higher as the older adult population was the primary population of interest rather than the general public.[52] In another study conducted by Mojtabai and Olfson,[3] they found that the long-term use of antidepressants may explain the recent increase of the overall antidepressant prescriptions in adults ages 18 and over. Future research is needed if the increasing rate of overall antidepressant prescriptions coincides with older adults' long-term use of antidepressants in office-based outpatient settings.

Second, the prevalence of potentially inappropriate antidepressant prescriptions among older adults in given all office-based outpatient visits remains stable around 1.0% across years. However, approximately one in 10 older adults with antidepressant-related visits is exposed to the potentially inappropriate antidepressant use. In other words, at least 2.2 million office-based outpatient visits made by older adults each year, on average, are at the risk of developing potentially avoidable drug-related adverse events. Some patterns were found in this prevalence. For instance, amitriptyline and doxepin were the two most frequent disease-independent antidepressants prescribed, accounting for more than 70% of the potentially inappropriate antidepressant prescriptions. This finding is supported by previous studies that these antidepressant agents are one of the most common causes for potentially inappropriate medication use in older adults.[27,53,54] Such a finding warrants that we should improve healthcare providers' prescribing practices to reduce potentially inappropriate antidepressant prescriptions. For example, education may help healthcare providers better understand that disease-independent and disease-dependent potentially inappropriate antidepressants should be avoided, even though the Beers Criteria and other guidelines do not always serve as a substitute for their judgment when prescribing. An alternative, possible explanation for this phenomenon is that healthcare providers do not feel the need to stop prescribing these medications as they work well for older patients that they see. Thus, future research is needed to qualitatively better understand the prescribing patterns of these medications among older patients.

Factors associated with the increased likelihood of visits involving overall antidepressant prescriptions among older adults included being female, seeing psychiatrists, and having mental health diagnoses and number of medications. The

finding posits a question whether or not female older adults are more receptive about antidepressants as a treatment option than their counterparts. In the case of the number of medications, it seems plausible as a previous study showed that antidepressants are one of the most common medications in older adults' polypharmacy.[46] Being ages 75 or older and racial/ethnic minorities were associated with the decreased likelihood of visits involving overall antidepressant prescriptions. As previous studies found,[55,56] racial/ethnic minorities may be under-treated with antidepressants among older adults.

Factors associated with the increased likelihood of visits involving potentially inappropriate antidepressant prescriptions among older adults who had antidepressant-related visits were: racial/ethnic minorities other than non-Hispanic Blacks and Hispanics, Medicaid as a primary source of payment, seeing psychiatrists, and the non-MSA status. In the case of racial/ethnic minorities and Medicaid beneficiaries, it appears that because they often have poor access to quality care and have lower quality of care for mental health conditions in general, they may also be exposed to a greater likelihood of potentially inappropriate antidepressant prescriptions. Future research is needed to address this issue. Surprisingly, the finding leaves a question about the relationship between seeing psychiatrists and potentially inappropriate antidepressant prescriptions. One possible explanation is that primary care providers may be more likely to adhere the guidelines related to potentially inappropriate antidepressant use than psychiatrists. Future research is needed to better understand the role of seeing psychiatrists versus primary care providers on the potentially inappropriate antidepressant prescriptions. With regards to the MSA status, future research is also needed if MSA-level geographic disparity exists in prescribing patterns of potentially inappropriate antidepressants across

the country. Finally, having more than five visits within the past 12 months and mental health diagnoses were associated with the decreased likelihood of such visits. It seems that those with frequent visits and mental health diagnoses may have received appropriate care, including appropriate antidepressant use.

This study is not without limitations. First, the NAMCS data capture up to three diagnoses in a sampled visit, and the survey response rate has declined in the last few years due to a redesign of sampling strategy. Such factors may cause underreporting potentially inappropriate antidepressant prescriptions due to drug-disease or drug-syndrome interactions. Second, when referrals are made across different healthcare providers, patient information is often lost.[57] Furthermore, healthcare providers may have refilled antidepressant prescriptions without coding the mental health diagnoses at each visit. This may also have led to underreporting of mental health diagnoses and potentially inappropriate antidepressant prescriptions. Third, there are potential confounders in multivariate logistic regression models. For example, socio-economic and other variables (e.g., education and marital status) are not collected. Interpretations of findings should consider these limitations.

Overall, our study highlights that the prevalence of overall antidepressant prescriptions in older adults continues to increase up to 10.1% in office-based outpatient visits, and the potentially inappropriate antidepressant prescriptions remain a persistent problem. Efforts to minimize potentially inappropriate antidepressant prescriptions may still be needed by providing educational interventions to healthcare providers, targeting specific antidepressant agents (e.g., amitriptyline and doxepin). To further guide policy changes, future research is also needed to evaluate factors that cause potentially

inappropriate antidepressant prescriptions in clinical practice. The on-going research will improve value-based quality of care among older adults who are prescribed antidepressants in office-based outpatient settings.

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Figure 3.1. National trends of antidepressant prescriptions among older adults in office-based outpatient settings, 2002-2012 NAMCS.

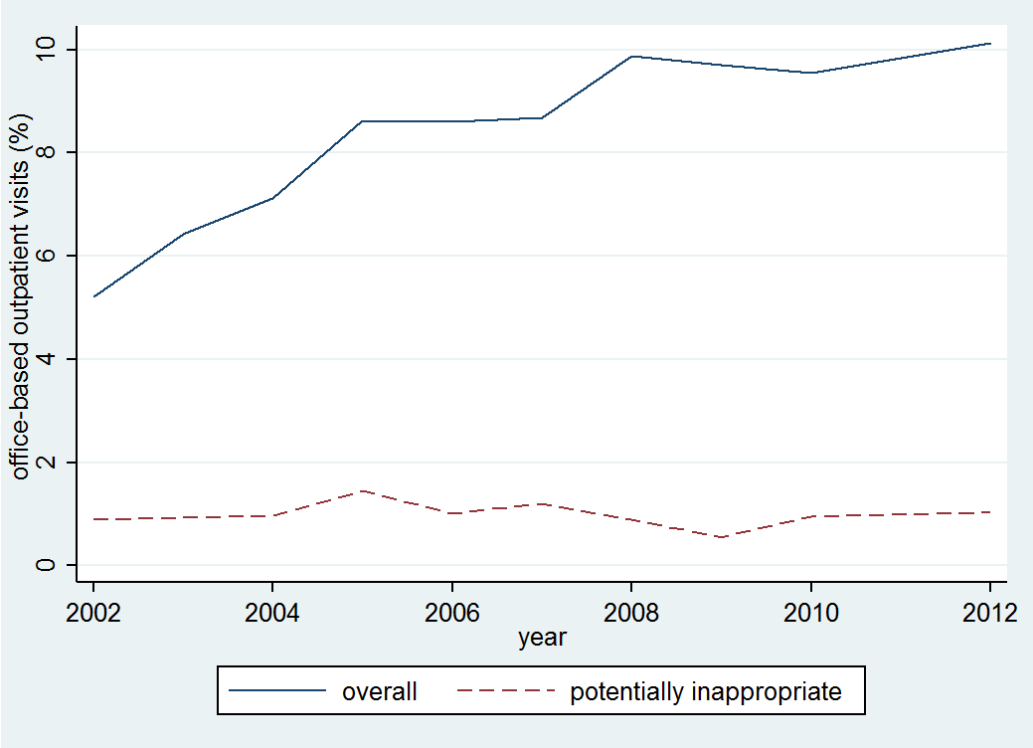

Figure 3.2. National trend of potentially inappropriate antidepressant prescriptions in given antidepressant-related visits, 2002-2012 NAMCS.

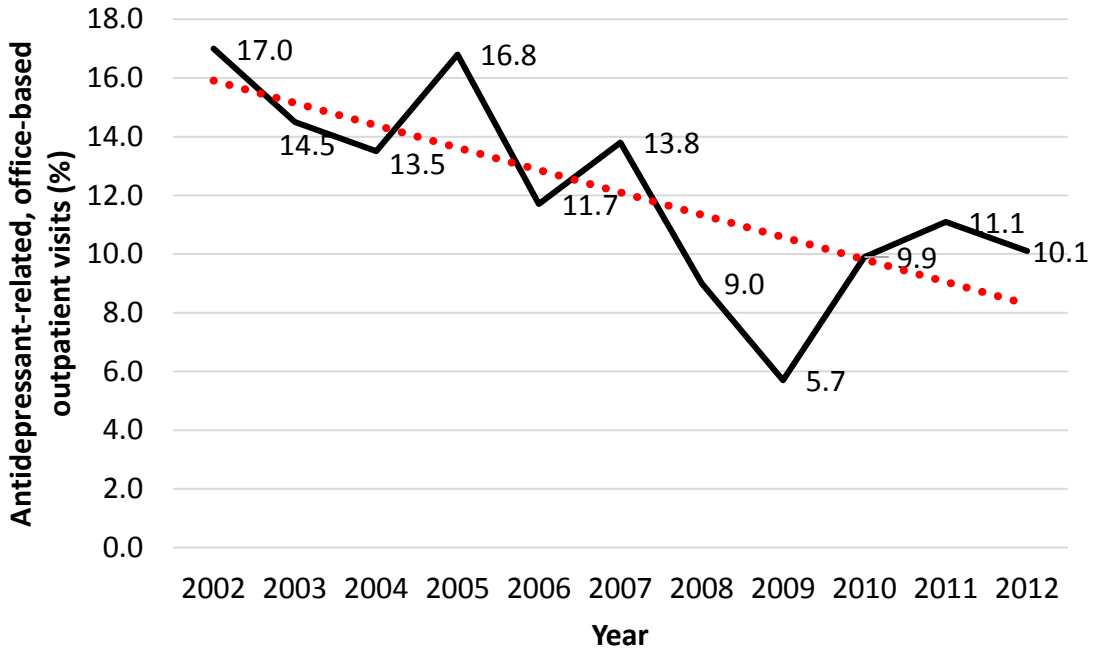

Table 3.1. Selected characteristics (weighted percent) of older adults in office-based outpatient settings by prescription status of antidepressant, 2009-2012 NAMCS.

	Antidepressant prescribed		Without antidepressants	Total	*P*-value‡
	Potentially inappropriate	Appropriate			
Age					
65-74	57.2	50.0	50.7	50.7	
75-84	32.3	36.3	36.0	36.0	0.4836
85+	10.5	13.8	13.3	13.3	
Gender					
Female	69.4	67.7	55.6	56.8	<0.0001
Male	30.6	32.4	44.4	43.2	
Race/ethnicity					
Non-Hispanic White	81.0	86.6	80.1	80.7	
Non-Hispanic Black	4.4	4.1	7.8	7.4	<0.0001
Hispanic	8.2	7.4	7.7	7.7	
Others[a)]	6.4	1.9	4.4	4.2	
Region					
Northeast	17.6	16.3	18.2	18.0	
Midwest	22.3	21.3	20.4	20.5	0.7941
South	40.9	38.8	38.4	38.5	
West	19.2	23.6	23.0	23.0	
Source of payment					
Medicare	80.0	81.1	81.2	81.1	
Medicaid	3.7	1.7	1.4	1.5	0.0149
Private	13.7	14.6	15.7	15.6	
Others[b)]	2.6	2.6	1.8	1.9	
Reason for visit					
Acute problem	26.4	23.7	25.9	25.7	
Routine chronic problem	54.0	59.8	53.7	54.3	0.0002
Preventive care	9.0	11.0	11.8	11.7	
Pre- or post-surgery	10.6	5.5	8.5	8.3	
Repeat of visits					
0 visit	6.5	5.9	7.8	7.6	
1-2 visits	32.4	28.5	35.4	34.7	<0.0001
3-5 visits	36.4	33.2	32.9	32.9	
6+ visits	24.7	32.3	24.0	24.7	
Physician specialty					
Primary care	50.8	50.2	38.9	40.1	
Psychiatry	5.2	7.3	0.5	1.1	<0.0001
Other specialties[c)]	44.1	42.5	60.6	58.8	
Type of medical practice					
Solo	91.6	89.6	92.6	92.3	0.0023
Others[d)]	8.4	10.4	7.4	7.7	
MSA status					

MSA	79.9	86.0	87.5	87.3	0.0471
Non-MSA	20.1	14.0	12.5	12.7	
Mental health diagnosis[e)]					
None / missing	91.6	76.1	96.6	94.7	
Major depression	2.0	3.4	0.1	0.5	
Dysthymia	1.2	1.8	0.1	0.3	
Other affective disorders	1.2	7.6	0.5	1.1	
Bipolar disorders	0.4	0.8	0.1	0.2	
Schizophrenia	0.6	0.4	0.1	0.1	
Delirium, dementia, and other cognitive deficits	0.2	2.5	0.7	0.8	<0.0001
Anxiety-related disorders	0.9	1.5	0.1	0.2	
Personality disorders	0.0	0.2	0.0	0.0	
Others	1.9	5.8	1.7	2.1	
Psychotherapy provided					
Yes	2.4	4.7	0.3	0.7	<0.0001
No	97.6	95.3	99.7	99.3	
Time spent with doctor					
< 15 min.	17.8	15.0	19.9	19.5	
15-20 min.	46.0	47.1	47.0	47.0	0.0013
21-30 min.	22.2	25.2	21.0	21.4	
> 30 min.	14.0	12.7	12.0	12.1	
Multiple chronic conditions (MCCs)					
None	7.4	7.5	16.4	15.5	
1	24.1	19.7	24.8	24.4	<0.0001
2-3	45.6	44.6	41.9	42.2	
4+	22.9	28.2	16.9	18.0	
Number of medications					
0	0.0	0.0	23.7	21.3	
1-2	4.6	8.2	25.5	23.8	<0.0001
3-5	23.5	20.3	21.4	21.3	
6+	71.9	71.5	29.4	33.6	
Sample size					
Unweighted sample	466	3,926	39,158	43,550	
Weighted population	2,259,397	22,189,574	220,872,034	245,321,006	

Note: ‡ Comparison across three groups. a) includes Asians, American Indian/Alaska Natives (AIANs), Native Hawaiian or Other Pacific Islanders (NHOPI), and multiple races; b) includes worker's compensation, self-pay, no charge, and others; c) includes general surgery, obstetrics/gynecology, orthopedic surgery, cardiovascular diseases, dermatology, urology, neurology, ophthalmology, otolaryngology, and others; d) includes federally qualified health center (FQHC), non-federal government clinic, family planning clinic, health maintenance organization (HMO) or other prepaid practice plan, and faculty practice plan; and e) refers to appendix 3.3.

Table 3.2. Prevalence of potentially inappropriate antidepressant prescriptions among older adults with antidepressant prescriptions in office-based outpatient visits, 2010-2012 NAMCS.

	Potentially inappropriate antidepressant prescription	
	No (n=3926)	Yes (n=466)
Regardless of diseases or conditions	**0.0%**	**97.2%**
Amitriptyline	0.0%	67.7%
Clomipramine	0.0%	5.9%
Doxepin	0.0%	15.4%
Imipramine	0.0%	8.3%
Trimipramine	0.0%	0.0%
Due to drug-disease or drug-syndrome interactions	**0.0%**	**8.2%**
Syncope x tertiary TCAs*	0.0%	0.1%
Seizure x bupropion or maprotiline	0.0%	0.0%
Delirium x anticholinergics	0.0%	0.0%
Dementia and cognitive impairment x anticholinergics	0.0%	0.0%
Constipation x tertiary TCAs or anticholinergics	0.0%	7.0%
Prostatic hyperplasia x anticholinergics	0.0%	1.1%

Note: *TCAs indicate tricyclics.

Table 3.3. Adjusted odds ratios (AOR) for prescribing antidepressants among older adults in office-based outpatient settings, NAMCS 2009-2012.

	Potentially inappropriate prescription of antidepressants[†]		Overall prescription of antidepressants[¶]	
	AOR	**95% CI**	**AOR**	**95% CI**
Age				
65-74	1.00		1.00	
75-84	0.84	0.60 - 1.18	0.85*	0.75 - 0.97
85+	0.76	0.45 - 1.28	0.75**	0.61 - 0.91
Gender				
Male	1.00		1.00	
Female	1.14	0.84 - 1.57	1.60***	1.43 - 1.78
Race/ethnicity				
Non-Hispanic White	1.00		1.00	
Non-Hispanic Black	1.17	0.58 - 2.35	0.44***	0.34 - 0.57
Hispanic	1.21	0.68 - 2.15	0.77*	0.61 - 0.96
Others[a)]	3.61**	1.49 - 8.72	0.47**	0.28 - 0.77
Region				
Northeast	1.00		1.00	
Midwest	1.01	0.63 - 1.63	0.97	0.80 - 1.18
South	1.04	0.68 - 1.59	1.16	0.97 - 1.40
West	0.82	0.54 - 1.25	1.16	0.93 - 1.45
Source of payment				
Medicare	1.00		1.00	
Medicaid	2.54*	1.04 - 6.18	1.33	0.96 - 1.86
Private	1.02	0.70 - 1.50	1.04	0.87 - 1.24
Others[b)]	1.25	0.61 - 2.55	1.12	0.81 - 1.55
Reason for visit				
Acute problem	1.00		1.00	
Routine chronic problem	0.89	0.63 - 1.28	0.97	0.85 - 1.11
Pre- or post-surgery	1.54	0.79 - 2.99	1.10	0.87 - 1.40
Preventive care	0.65	0.40 - 1.06	0.91	0.78 - 1.06
Repeat of visits				
0 visit	1.00		1.00	
1-2 visits	0.75	0.42 - 1.34	0.93	0.74 - 1.15
3-5 visits	0.76	0.44 - 1.33	0.94	0.71 - 1.24
6+ visits	0.54*	0.31 - 0.95	1.09	0.85 - 1.41
Physician specialty				
Primary care	1.00		1.00	
Psychiatry	3.97**	1.53 - 10.33	10.71***	5.67 - 20.21
Other specialties[c)]	0.81	0.57 - 1.16	0.90	0.79 - 1.03
Type of medical practice				
Solo	1.00		1.00	
Others[d)]	0.73	0.47 - 1.14	1.17	0.96 - 1.43

MSA status				
MSA	1.00		1.00	
Non-MSA	1.93**	1.19 - 3.13	0.94	0.74 - 1.18
Mental health diagnosis[e)]				
No / missing	1.00		1.00	
Yes	0.17***	0.09 - 0.32	5.78***	4.61 - 7.23
Psychotherapy provided				
No	1.00		1.00	
Yes	0.55	0.22 - 1.36	1.58	0.94 - 2.66
Time spent with doctor				
< 15 min.	1.00		1.00	
15-20 min.	0.90	0.60 - 1.37	1.10	0.94 - 1.29
21-30 min.	0.82	0.50 - 1.35	1.10	0.92 - 1.32
> 30 min.	0.98	0.58 - 1.67	0.95	0.75 - 1.19
Multiple chronic conditions (MCCs)				
None	1.00		1.00	
1	1.42	0.81 - 2.49	1.07	0.85 - 1.35
2-3	1.18	0.69 - 2.00	1.07	0.85 - 1.35
4+	0.87	0.53 - 1.41	1.24	0.95 - 1.63
Number of medications				
0-2	1.00		1.00	
3-5	1.66	0.95 - 2.92	8.03***	6.29 - 10.25
6+	1.36	0.72 - 2.56	23.35***	18.87 - 28.90
Survey year				
2009	1.00		1.00	
2010	1.85*	1.11 - 3.08	1.04	0.89 - 1.22
2011	2.16**	1.32 - 3.53	1.01	0.85 - 1.20
2012	1.92**	1.26 - 2.93	1.15	0.98 - 1.34
Sample size				
Unweighted sample		4,392		43,550
Weighted population		24,448,971		245,321,006
F-statistic		4.33***		76.65***

Note: † the denominator is antidepressant-related visits, and ¶ the denominator is all visits. * <0.05; **<0.01; ***<0.001. a) includes Asians, American Indian/Alaska Natives (AIANs), Native Hawaiian or Other Pacific Islanders (NHOPI), and multiple races; b) includes worker's compensation, self-pay, no charge, and others; c) includes general surgery, obstetrics/gynecology, orthopedic surgery, cardiovascular diseases, dermatology, urology, neurology, ophthalmology, otolaryngology, and others; d) includes federally qualified health center (FQHC), non-federal government clinic, family planning clinic, health maintenance organization (HMO) or other prepaid practice plan, and faculty practice plan; and e) refers to appendix 3.3.

Appendix 3.1. Antidepressant medications by class[29]

Tricyclics (TCAs)
- Amitriptyline[a), b), f)]
- Amoxapine[b)]
- Clomipramine[a), b), f)]
- Desipramine[b)]
- Doxepin[a), b), f)]
- Imipramine[a), b), f)]
- Maprotiline
- Nortriptyline[b)]
- Protriptyline[b)]
- Trimipramine[a), b), f)]

Serotonin Modulators
- Nefazodone
- Trazodone
- Vilazodone[e)]
- Vortioxetine[e)]

Selective Serotonin Reuptake Inhibitors (SSRIs)
- Citalopram
- Escitalopram
- Fluoxetine
- Fluvoxamine
- Paroxetine[b)]
- Sertraline

Monoamine Oxidase Inhibitors (MAOIs)
- Isocarboxazid
- Phenelzine
- Tranylcypromine
- Rasagiline[c)]
- Selegiline[c)]

Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)
- Desvenlafaxine
- Duloxetine
- Levomilnacipran[e)]
- Venlafaxine
- Milnacipran[d)]

Miscellaneous
- Bupropion
- Mirtazapine

Note: a) denotes tertiary TCAs; b) denotes drugs with strong anticholinergic properties; c) denotes a MAO-B inhibitor and is primarily classified as anti-Parkinsonian agents; d) is primarily classified as fibromyalgia agents; e) indicates that it is not available in NAMCS; and f) indicates that it should be avoided, or potentially inappropriate, regardless of diagnosis, according to 2012/2015 Beers criteria.

Appendix 3.2. 2012/2015 Beers criteria for potentially inappropriate antidepressant use in older adults due to drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome[5-6]

Disease or syndrome (ICD-9-CM code)	Antidepressant[a)]	Rationale	Recommendation	Quality of Evidence	Strength of recommendation
Cardiovascular					
Syncope (780.2, 992.1)	Tertiary TCAs	Increase risk of orthostatic hypotension or bradycardia	Avoid	Moderate	Strong
Central nervous system					
Chronic seizures or epilepsy (345, 780.33)	bupropion; maprotiline	Lowers seizure threshold; may be acceptable in patients with well-controlled seizures in whom alternative agents have not been effective	Avoid	Moderate	Strong
Delirium (290.11, 290.3, 290.41, 291.0, 292.81, 293.0, 293.1)	TCAs; Anticholinergics	Induce or worsen delirium in older adults; if discontinuing drugs used chronically, taper to avoid withdrawal symptoms	Avoid	Moderate	Strong
Dementia and cognitive impairment (290, 291.2, 292.82, 294.10, 294.11, 294.20, 294.21, 331.0, 331.19, 331.82, 331.83)	Anticholinergics	Avoid because of adverse CNS effects	Avoid	High	Strong
History of falls or fractures (E880-E888)[b)]	TCAs; SSRIs	Ability to produce ataxia, impaired psychomotor function, syncope, and additional falls	Avoid unless safer alternatives are not available	High	Strong
Gastrointestinal					
Chronic constipation (564)	Tertiary TCAs; Anticholinergics	Can worsen constipation	Avoid unless no other alternatives	Moderate to low	Weak
Lower urinary tract symptoms, benign prostatic hyperplasia (600)	Anticholinergics	May decrease urinary flow and cause urinary retention	Avoid in men	Moderate	Inhaled agents: strong; others: weak

Note: a) refers to appendix 3.1 for full description; and b) excluded in the analysis for consistency, as NAMCS only collected external cause information using ICD-9-CM in 2002-2004.

Appendix 3.3. Mental health diagnosis[46]

Diagnosis	ICD-9-CM diagnostic code (290-319)
Affective disorder	
Major depression	296.2 & 296.3
Dysthymia	300.4
Other affective disorder	296.1, 296.81, 296.82, 296.9, & 311.0
Bipolar disorder	
Bipolar disorder	296.00-296.06, 296.40-296.46, 296.50-296.56, 296.60-296.66, 296.7, 296.80, 296.89
Schizophrenia	
Schizophrenia	295
Delirium, dementia, and other cognitive impairment	
Delirium	290.11, 290.3, 290.41, 291.0, 292.81, 293.0, 293.1
Dementia and other cognitive impairment	290, 291.2, 292.82, 294.10, 294.11, 294.20, 294.21, 331.0, 331.19, 331.82, 331.83
Anxiety Disorders	
Generalized anxiety disorder (GAD)	300.02
Panic disorder with or without agoraphobia	300.01 & 300.21
Obsessive-compulsive disorder	300.3
Personality Disorders	
Personality disorders	301
Others	Otherwise

Appendix 3.4. National trends of antidepressant prescriptions among older adults in office-based outpatient settings, 2002-2012 NAMCS.

Year	Overall prescription of antidepressants (95% CI)	Overall potentially inappropriate prescription of antidepressants (95% CI)	Potentially inappropriate use of antidepressants among antidepressant-related visits (95% CI)
2002	5.2 % (4.34, 6.27)	0.9% (0.66, 1.20)	17.0% (13.11, 21.81)
2003	6.4% (5.30, 7.75)	0.9% (0.65, 1.33)	14.5% (10.54, 19.58)
2004	7.1% (5.73, 8.83)	1.0% (0.62, 1.48)	13.5% (9.42, 19.00)
2005	8.6% (7.30, 10.18)	1.5% (0.98, 2.13)	16.8% (12.27, 22.45)
2006	8.6% (7.48, 9.90)	1.0% (0.77, 1.32)	11.7% (9.09, 14.99)
2007	8.7% (7.50, 10.05)	1.2% (0.91, 1.57)	13.8% (10.84, 17.32)
2008	9.9% (8.71, 11.18)	0.9% (0.63, 1.24)	9.0% (6.64, 12.05)
2009	9.7% (8.51, 11.06)	0.6% (0.38, 0.81)	5.7% (3.99, 8.07)
2010	9.6% (8.34, 10.95)	1.0% (0.67, 1.34)	9.9% (7.08, 13.76)
2011	10.0% (8.73, 11.37)	1.1% (0.77, 1.60)	11.1% (7.76, 15.72)
2012	10.1% (9.30, 11.03)	1.0% (0.85, 1.24)	10.1% (8.46, 12.11)
Total	8.5% (8.08, 9.03)	1.0% (0.88, 1.09)	11.5% (10.51, 12.54)
P-value	<0.0001	0.0773	<0.0001

CHAPTER 4

Manuscript #2: Impacts of the 2009 USPSTF Depression Screening Recommendation on Diagnosing and Treating Mental Health Conditions: A Difference-in-Differences (DID) Analysis

Keywords: depression screening, depression, antidepressant, older adults, primary care

Abstract text word count: 177 (≤ 200)
Article text word count: 2,896 (≤ 3,000)
Number of tables: 2
Number of figures: 0
Number of appendices: 3

Joint Acknowledgment/Disclosure Statement: Dr. Rhee conceived the study, acquired data, analyzed and interpreted the data, led the writing of the manuscript, and oversaw every aspect of the study. Drs. Capistrant, Schommer, Hadsall, and Uden contributed to the interpretation of the data, and critically revised the manuscript.

Funding Source: As part of authors' regular salary and fringe benefits, different departments from the University of Minnesota provided financial support for this study. This funding arrangement ensured the authors' independence in writing and publishing this original research.

Conflict of Interest: The authors declare that they do not have a conflict of interest.

Disclaimers: Publicly available data were obtained from the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC). Analyses, interpretation, and conclusions are solely those of the authors and do not necessarily reflect the views of the Division of Health Interview Statistics or NCHS of the CDC.

Compliance with Ethical Standards: Using publicly available de-identified data, the research procedure for this study was exempted from the University of Minnesota Institutional Review Board.

ABSTRACT

Objective: To examine the impact of 2009 U.S. Preventive Services Task Force (USPSTF) depression screening recommendation on the following three outcomes: diagnoses of depression and other mood disorders; antidepressant prescriptions; and provision of non-pharmacological psychiatric services after controlling for covariates among older adults (ages 65+) in office-based outpatient primary care settings.

Data Source: 2006-2012 National Ambulatory Medical Care Survey (NAMCS) data, a nationally representative sample of office-based outpatient primary care visits among older adults (n= 15,596 unweighted).

Study Design: Using a multivariate difference-in-differences analysis, we estimated impacts of the USPSTF depression screening recommendation on aforementioned outcomes by comparing pre- (2006-2009) and post- (2010-2012) periods.

Principal Findings: Visits associated with a diagnosis of mood disorders other than depression differentially decreased by 18.8 percentage points (95% CI: -31.1, -6.5; p=0.003). No differential impact was found in other outcomes.

Conclusions: The 2009 USPSTF depression screening recommendation resulted in a decreased rate of diagnosing mood disorders other than depression, but had no impact on prescribing patterns of antidepressants and provision of non-pharmacological psychiatric services among older adults in office-based outpatient settings.

Word Count: 177

4.1 Introduction

In 2013, approximately 15.7 million U.S. adults ages 18 and over had at least one major depressive episode in the past year (Substance Abuse and Mental Health Services Administration 2014). In addition, 6.7% of U.S. adults experience major depressive disorder (hereafter referred to as depression) each year (National Institute of Mental Health 2015). While aging-related depression is a leading cause of disability and a major contributor for disease burden (World Health Organization 2015), depression and other related mood disorders (e.g., dysthymia) are often under-diagnosed and under-treated among adults ages 65 and over (hereafter referred to as older adults) (Wiese 2011). While adults with depression are not likely to make psychiatry-related visits, they still seek care in primary care or other specialty visits, making "these visits particularly important opportunities to detect and initiate treatment of depression" (Palmer and Coyne 2003, p.279). In light of providing care for depression in primary care and other specialty visits, screening for depression has become a "prominent component of the "detect—treat—improve" paradigm for undetected depression" since mid-1990s (Palmer and Coyne 2003, p.280).

In 2002, the U.S. Preventive Services Task Force (USPSTF) recommended depression screening for all eligible adults (U.S. Preventive Services Task Force 2002). Subsequently, the 2009 USPSTF practice recommendation stated depression screening should be provided in eligible adults to "ensure accurate diagnosis, effective treatment and appropriate follow-up" related to depression and other mental health conditions (U.S. Preventive Services Task Force 2009; U.S. Preventive Services Task Force 2015). Unlike the previous 2002 version, the 2009 USPSTF guideline distinguished two different

recommendations: a grade B recommendation is given when staff-assisted depression care supports are in place, and a grade C recommendation is given when staff-assisted depression care supports are not present in primary care settings (U.S. Preventive Services Task Force 2015). Unlike the grade B recommendation, the grade C recommendation indicates that the USPSTF makes no recommendation for or against routine depression screening service, and the service may be provided based on professional judgment and/or patient preferences (U.S. Preventive Services Task Force 2015). In 2016, the USPSTF disseminated its updated recommendation, which remains unchanged that a grade B recommendation is given regardless of staff-assisted depression care supports status (Siu et al. 2016; U.S. Preventive Services Task Force 2016).

In existing literature, there are few studies that assess the policy impact of recent USPSTF guidelines (e.g., mammography use (Block et al. 2013) and pediatric urinalysis (Filice et al. 2014)). However, no study has yet assessed the impact of the 2009 depression screening recommendation, including among older adults ages 65 and over. Gaps remain in our understanding of whether the 2009 depression screening recommendation had impacts on the following outcomes: diagnoses of depression and other mood disorders; overall and potentially inappropriate antidepressant prescriptions; and provision of non-pharmacological psychiatric services among older adults ages 65 and over. To address these gaps, we examine the policy impacts of the 2009 USPSTF depression screening recommendation on the aforementioned outcomes between pre- (2006-2008) and post- (2010-2012) periods among older adults, who made office-based outpatient primary care visits.

4.2 Methods

Data Source and Study Sample

We used data from 2006-2012 National Ambulatory Medical Care Survey (NAMCS), which are administrated by National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) (National Center for Health Statistics 2009). The NAMCS is an annual, cross-sectional survey of visits to office-based physicians in outpatient settings, and provides reliable information about the provision and/or use of ambulatory medical care services in the United States (National Center for Health Statistics 2009). Our final analytic sample included older adults ages 65 and over, who had primary care visits, and had completed data for all covariates (n=15,596 unweighted). Using publicly available data, the research procedure for this study was exempted from the University of Minnesota Institutional Review Board. Further details of the survey, including descriptions, questionnaires, sampling methodology and datasets, are publicly available on the NAMCS website (National Center for Health Statistics 2015).

Measures

Dependent variables. Three main outcomes of interests are as follow: diagnosis of mental health conditions, antidepressant prescription, and provision of non-pharmacological psychiatric services. First, we included the diagnosis of mental health conditions (i.e., depression only, mood disorders other than depression, and any mood disorders) (see Appendix 4.1 (Finkelstein, Prabhu, and Chen 2007). The NAMCS collects up to three clinical diagnoses using the *International Classification of Diseases, 9th edition, clinical*

modification (ICD-9-CM) diagnostic codes. We constructed three binary variables (yes or no/missing) for diagnosis of mental health conditions, and they are depression only, mood disorders other than depression, and overall, any mood disorders.

Second, antidepressant prescription was another outcome measure. The NAMCS collects up to eight medications in 2006-2011 and up to 10 medications in 2012. Using the *2015 American Hospital Formulary Service (AHFS) Compendium* (American Society of Health-System Pharmacists 2015), Wolters Kluwer's *Drug Facts and Comparisons* (Wolters Kluwer Clinical Drug Information 2015), and previous studies (Lindsey 2009; Mamdani et al. 2000; Maust, Oslin, and Marcus 2014; Mort and Aparasu 2000; Olfson and Marcus 2009; Sclar et al. 2012), we identified prescribed antidepressant medications using generic names (see Appendix 4.2). We constructed a binary variable (yes or no) for overall antidepressant prescriptions. For potentially inappropriate antidepressant prescriptions, we constructed a binary variable (yes or no) using the 2012/2015 Beers Criteria (see Appendices 4.2 and 4.3 (American Geriatrics Society Beers Criteria Update Expert Panel 2012, 2015)).

Third, we included non-pharmacological psychiatric service use as an outcome measure. The NAMCS asks two questions whether psychotherapy and mental health counseling other than psychotherapy were provided (yes or no) (National Center for Health Statistics 2010). Due to limited sample size, a binary variable (yes or no) was created aggregating these two questions.

Independent variables. The key exposure of interest was the depression screening status (yes or no). More specifically, the NAMCS asks, "Was the depression screening exam

ordered or provided at the visit?" The time indicator variable was also included to identify before and after the 2009 USPSTF depression screening guideline (0=2006-2008 (known as a reference category) and 1=2009-2012).

Control variables. Based on previous studies (Aparasu, Jano, and Bhatara 2009; Comer, Mojtabai, and Olfson 2011; Daumit et al. 2002; Harrison et al. 2010; Jameson and Blank 2010; Lagomasino, Stockdale, and Miranda 2011; Manseau and Case 2014; Maust et al. 2014; Mojtabai and Olfson 2010; Mort and Aparasu 2000; Olfson and Marcus 2009; Sankaranarayanan and Puumala 2007), we identified a number of covariates. We included demographic variables: age (65-74, 75-84, or 85+), gender, race/ethnicity, region (Northeast, Midwest, South, or West), primary source of payment (Medicare, Medicaid, private, or others), reason for visit (acute problem, routine chronic problem, preventive care, or pre- or post-surgery care), and repeat of visits within the past 12 months (none, 1-2, 3-5, or 6+). In addition, we included the following clinical characteristics: type of medical practice (solo or others), metropolitan statistical area (MSA) status (yes or no), time spent with doctor (<15, 15-20, 21-30, or >30 min.), number of chronic conditions (none, 1, 2-3, or 4+), and number of medications (0-2, 3-5, or 6+). The number of chronic conditions was based on 14 chronic conditions (yes or no) collected by the NAMCS (e.g., arthritis, congestive heart failure, and diabetes) (National Center for Health Statistics 2010). The variable, repeat of visits, had the largest missing proportion (14.8%), and was imputed based on age, gender and the number of medications using the *hotdeck* imputation technique (Mander and Clayton 2007). Other variables that had missing values included: primary source of payment (3.9%), reason for

visit (1.7%), and the number of chronic conditions (1.2%). Observations with all of these missing values (6.5%) were systematically excluded, leaving the final sample size of 15,596 visits (unweighted).

Data Analysis

First, we examined the extent to which demographic and clinical characteristics differed in older adults by the depression screening status. We used cross-tabulations and design-based *F*-tests to investigate differences by the depression screening status. Second, we employed a series of difference-in-differences (DID) models to investigate if the 2009 USPSTF depression screening recommendation had differential impacts on three aforementioned different outcomes. This was done by regressing each outcome on the indicator variable of depression screening status (yes or no), a time indicator variable (before 2009 (i.e., 2006-2008) or after 2009 (i.e., 2010-2012)), and the interaction of these two variables, while adjusting for all other covariates. We used Stata 13.1 (StataCorp. 2013) for all analyses and the *svy* commands in Stata were employed to account for the complex sample design of the NAMCS (i.e., unequal probability of selection, clustering and stratification).

4.3 Results

Characteristics of the Study Sample

Table 4.1 presents demographic and clinical characteristics of older adults in office-based outpatient primary care visits by the depression screening status before the implementation of 2009 USPSTF depression screening recommendation (2006-2008).

All outcomes of interest had significant differences by the depression screening status (p<0.0001). 44.0% of older adults, who had a depression screening exam during their office-based outpatient primary care visits, were also diagnosed with some form of mental health conditions (p<0.0001). It is also noteworthy that about 30.0% of older adults who received a depression screening exam also had antidepressant prescriptions (p<0.0001). For non-pharmacological psychiatric services, 4.8% and 6.0% of older adults, who received the depression screening exam, had psychotherapy and mental health counseling other than psychotherapy, respectively (p<0.0001).

For demographic characteristics, age, gender, race/ethnicity, and other factors were not significantly differed by the depression screening status. Unlike demographic characteristics, however, most of clinical characteristics had significant differences by the depression screening status. For example, among older adults who had depression screening exam, the majority (95.6%) had solo as type of medical practice (p=0.0427). For time spent with doctor, 57.6% of older adults, who had the depression screening exam, spent at least 21 minutes with their doctors, and this is comparable to those who did not receive the depression screening exam (22.7%) (p<0.0001). For multiple chronic conditions, 73.7% of older adults, who received the depression screening exam, had with at least two conditions, which is significantly higher than those who did not receive the depression screening exam (67.0%) (p=0.0038). Lastly, for the number of medications prescribed, 78.4% of older adults, who had the depression screening exam, had at least three medications prescribed, and this is significantly higher than those who did not have the depression screening exam (62.8%) (p=0.0003).

<Table 4.1 about here>

Difference-in-Differences

Table 4.2 presents the adjusted prevalence of selected outcomes among older adults in their office-based outpatient primary care visits by depression screening status and the time period. Overall, the prevalence of diagnosis with any mood disorders significantly decreased from 43.6% in pre-2009 to 26.6% in post-2009 among older adults who had the depression screening exam in their visits. On the other hand, the prevalence of diagnosis with any mood disorders increased from 6.0% in pre-2009 to 7.1% in post-2009 among older adults who did not have the depression screening exam in their visits. Differences by the time period indicate that -37.6% among the pre-2009 and -19.5% among the post-2009, resulting in a differential impact of -18.1% (95% CI: -30.9, -5.2; p=0.006). According to the sub-group analysis, such differential impact is largely due to the diagnosis of mood disorders other than depression, which had the differential impact of -18.8% (95% CI: -31.1, -6.5; p=0.003), rather than depression itself (p=0.608). No differential impact due to the 2009 USPSTF depression screening recommendation was found in the cases of antidepressant prescription patterns (p=0.680) and the utilization of psychiatric services (p=0.679).

<Table 4.2 about here>

4.4 Discussion

This is one of the first population-based observational studies to examine the impact of the 2009 USPSTF depression screening recommendation among older adults in office-based outpatient settings. Overall, significant reductions were found in diagnoses of mood disorders other than depression and overall mood disorders. On the other hand, a

slight increase in the diagnosis rate of depression was found due to the depression screening recommendation, but it was not statistically significant. Finally, no differential impact was found in terms of prescribing patterns of antidepressants and provision of non-pharmacological psychiatric services.

First, an increased rate of depression diagnosis was found, while it was not statistically significant. This finding is consistent with previous studies that show no or uncertain improvement of depression-related outcomes due to depression screening (Thombs and Ziegelstein 2014; Thombs et al. 2014). It may be due to a broadly defined guideline in the USPSTF depression screening recommendation statements, which do not specify which depression screening instruments should be used in primary care settings. This implies that primary care patients may be asked as few as two questions suggested by Whooley and her colleagues (Whooley et al. 1997), or other comprehensive tools, such as a 9-item Patient Health Questionnaire (PHQ-9) (Moriarty et al. 2015; Spitzer, Kroenke, and Williams 1999), and Kessler psychological distress scale (Kessler et al. 2002) among others (Bland and Streiner 2013; Maurer 2012). Due to heterogeneity of various depression screening tools that may be used across diverse primary care practices, it is possible that only a slightly increased rate, which was not statistically significant, of depression diagnosis was observed.

According to the American Geriatrics Society, PHQ-2 is recommended as an initial depression screening tool, and a 15-item Geriatric Depression Scale as a follow-up test for older adults (Maurer 2012). It remains unclear whether this study's findings would have been different if only these two specific instruments were used in this

specific population of interest. Future research needs to elucidate the roles of specific depression screening tools on the depression diagnosis in this specific population group.

Second, we found a significant decrease in the rate of diagnoses of mood disorders other than depression. One of possible reasons is the quality of depression screening tools. For example, false-positive rates of existing screening tools are relatively high (Bland and Streiner 2013), such that primary care providers do not order follow-up tests for mental health diagnoses other than depression. Alternatively, another possible reason is that primary care providers may not be well-informed about procedures when several screening tools are available with little evidence of such tools (Bland and Streiner 2013). Future research needs to address if significant reductions in the rate of diagnosing mood disorders other than depression are due to selectivity of depression screening tools and/or practicing patterns (e.g., knowledge) among primary care providers.

Third, no differential impact was found for prescribing patterns of antidepressants and provision of non-pharmacological psychiatric services. It is not surprising given that no significant increase in the rate of depression diagnosis and a significant decrease in the rate of diagnoses of mood disorders other than depression were found in this study. Such a finding, however, does not endorse casual relationships among depression screening, diagnoses and treatments of depression and other mood disorders. Future research is needed to characterize casual pathways for depression screening, diagnoses and treatments of depression and other mood disorders; such findings can further guide the effectiveness of a depression screening guideline.

The study has several limitations. First, unlike the 2002 and 2016 versions, the 2009 USPSTF depression screening recommendation distinguishes that use of the

screening service is recommended if and only if staff-assisted depression care supports are in place (i.e., grade B recommendation). Otherwise, the screening service may only be provided depending on individual circumstances (i.e., grade C recommendation) (U. S. Preventive Services Task Force 2009). Because the NAMCS does not collect information regarding staff-assisted depression care supports, careful interpretations of the study findings are needed. In other words, the study assumes that depression screening was provided whether staff-assisted depression care supports were in place or not when it was given. Currently, no publicly available national data allow us to collect such information.

Second, the unit of analysis in this study was patient visits, not individual patients. This may have resulted in differential estimates when compared to other patient-based studies. In addition, detailed depression screening strategies are not known in the NAMCS. For instance, future research should address such issues (e.g., types and intensity of depression screening) when examining the roles of depression screening on diagnosing and treating depression and other mental health conditions.

Strengths of the study include the use of a quasi-experimental difference-in-differences method (Khandker, Koolwal, and Samad 2010) to evaluate the impact of the 2009 depression screening recommendation at a national level. In particular, the research design accounted for secular time trends in the use of depression screening and differential time trends in unobserved control variables (Khandker et al. 2010). This study adds value to existing literature because no population-based observational study was conducted to support previous studies, as they solely used a randomized controlled trial approach (O'Connor et al. 2009; Thombs et al. 2013; Thombs et al. 2014).

In conclusion, the study provides pioneering evidence that the 2009 USPSTF depression screening recommendation resulted in a decreased rate of diagnosing mood disorders other than depression, but had no impact on prescribing patterns of antidepressants and provision of non-pharmacological psychiatric services among older adults in office-based outpatient settings. As for policy implications, the Canadian Task Force on Preventive Health Care recommended against depression screening in 2013 because no RCT study supports the effectiveness of depression screening on depression outcomes in primary care settings (Thombs and Ziegelstein 2013). Currently, the 2016 USPSTF recommendation remains unchanged in the U.S. More population-based observational research, which eventually overcomes current limitations, is needed in the near future to strengthen and support current USPSTF depression screening recommendation statements.

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Table 4.1. Selected baseline characteristics (weighted percent) of older adults in office-based outpatient primary care settings by depression screening, 2006-2008 NAMCS.

	Depression screening		Total	*P*-value
	No	Yes		
Mental health diagnosis[a)]				
None/missing	93.8	56.0	93.1	<0.0001
Yes	6.2	44.0	6.9	
Antidepressant prescription				
No	88.5	69.9	88.1	
Yes, appropriate	10.1	29.6	10.4	<0.0001
Yes, potentially inappropriate	1.5	0.6	1.5	
Psychotherapy provided				
Yes	0.1	4.8	0.2	<0.0001
No	99.9	95.2	99.8	
Mental health counseling provided (excluding psychotherapy)				
Yes	0.4	6.0	0.5	<0.0001
No	99.6	94.0	99.5	
Age				
65-74	49.5	55.7	49.7	
75-84	36.9	32.6	36.8	0.4851
85+	13.6	11.7	13.6	
Gender				
Female	59.8	63.2	59.9	0.5555
Male	40.2	36.8	40.1	
Race/ethnicity				
Non-Hispanic White	77.8	83.3	77.9	
Non-Hispanic Black	9.4	5.9	9.4	0.3244
Hispanic	8.2	9.7	8.3	
Others[b)]	4.6	1.1	4.5	
Region				
Northeast	16.7	31.7	17.0	
Midwest	19.8	17.5	19.7	0.0508
South	43.4	44.5	43.4	
West	20.1	6.4	19.8	
Source of payment				
Private	17.1	18.1	17.2	
Medicare	75.8	78.7	75.9	0.4228
Medicaid	4.9	2.8	4.9	
Others[c)]	2.1	0.3	2.1	
Reason for visit				
Acute problem	32.7	20.6	32.5	
Routine chronic problem	50.8	55.1	50.9	0.0730
Preventive care	14.1	23.9	14.3	
Pre- or post-surgery	2.4	0.5	2.3	

Repeat of visits				
0 visit	2.7	4.8	2.7	
1-2 visits	23.7	27.6	23.7	0.3260
3-5 visits	38.8	42.7	38.9	
6+ visits	34.8	24.9	34.6	
Type of medical practice				
Solo	88.9	95.6	89.0	0.0427
Others[d)]	11.1	4.5	11.0	
MSA status				
MSA	80.4	90.7	80.6	0.0824
Non-MSA	19.6	9.3	19.4	
Time spent with doctor				
< 15 min.	15.1	4.1	14.8	
15-20 min.	62.3	38.4	61.8	<0.0001
21-30 min.	16.0	28.1	16.2	
> 30 min.	6.7	29.5	7.1	
Multiple chronic conditions (MCCs)				
None	11.3	2.3	11.1	
1	21.8	23.9	21.8	0.0038
2-3	47.5	42.4	47.4	
4+	19.5	31.4	19.7	
Number of medications				
0	12.0	3.2	11.8	
1-2	25.2	18.3	25.1	0.0003
3-5	29.1	47.2	29.4	
6+	33.7	31.2	33.7	
Sample size				
Unweighted sample	6,169	114	6,283	
Weighted population	92,405,865	1,768,751	93,590,045	

Note: a) refers to appendix 4.1; b) includes Asians, American Indian/Alaska Natives (AIANs), Native Hawaiian or Other Pacific Islanders (NHOPI), and multiple races; c) includes worker's compensation, self-pay, no charge, and others; and d) includes federally qualified health center (FQHC), non-federal government clinic, family planning clinic, health maintenance organization (HMO) or other prepaid practice plan, and faculty practice plan.

Table 4.2. Adjusted proportion of selected outcomes among older adults in office-based outpatient primary care settings by depression screening, NAMCS 2006-2012.

	With depression screening (%)		Without depression screening (%)		Difference (%)		Difference-in-Differences (%)		
	Pre-2009	Post-2009	Pre-2009	Post-2009	Pre-2009	Post-2009	b	95% CI	*P*-value
Mental health diagnosis									
Diagnosed with any mood disorder(s)	43.6	26.6	6.0	7.1	-37.6	-19.5	-18.1	(-30.9, -5.2)	0.006
Diagnosed with depression	1.3	2.2	0.0	0.1	-1.3	-2.1	0.8	(-2.1, 3.6)	0.608
Diagnosed with mood disorders other than depression	42.3	24.4	6.0	6.9	-36.3	-17.5	-18.8	(-31.1, -6.5)	0.003
Antidepressant prescription									
Prescribed with any antidepressant(s)	28.2	25.8	10.9	10.8	-17.3	-15.0	-2.3	(-13.1, 8.5)	0.680
Prescribed with potentially inappropriate antidepressants	0.5	-0.1	1.6	1.4	1.1	1.5	-0.4	(-1.8, 0.8)	0.463
Psychiatric service use									
Provided with psychotherapy or other mental health counseling	9.1	10.9	0.4	0.4	-8.7	-10.5	1.8	(-6.6, 10.1)	0.679
Sample size									
Unweighted sample	323		15,273					15,596	
Weighted population	1,748,058		91,841,986					93,590,045	

Note: controlled for all other covariates.

Appendix 4.1. Mental health diagnosis

Diagnosis	ICD-9-CM diagnostic code (290-319)
Affective disorder	
Major depression	296.2 & 296.3
Dysthymia	300.4
Other affective disorder	296.1, 296.81, 296.82, 296.9, & 311.0
Bipolar disorder	
Bipolar disorder	296.00-296.06, 296.40-296.46, 296.50-296.56, 296.60-296.66, 296.7, 296.80, 296.89
Schizophrenia	
Schizophrenia	295
Delirium, dementia, and other cognitive impairment	
Delirium	290.11, 290.3, 290.41, 291.0, 292.81, 293.0, 293.1
Dementia and other cognitive impairment	290, 291.2, 292.82, 294.10, 294.11, 294.20, 294.21, 331.0, 331.19, 331.82, 331.83
Anxiety Disorders	
Generalized anxiety disorder (GAD)	300.02
Panic disorder with or without agoraphobia	300.01 & 300.21
Obsessive-compulsive disorder	300.3
Personality Disorders	
Personality disorders	301
Others	Otherwise

Appendix 4.2. Antidepressant medications by class

Tricyclics (TCAs)
- Amitriptyline[a), b), f)]
- Amoxapine[b)]
- Clomipramine[a), b), f)]
- Desipramine[b)]
- Doxepin[a), b), f)]
- Imipramine[a), b), f)]
- Maprotiline
- Nortriptyline[b)]
- Protriptyline[b)]
- Trimipramine[a), b), f)]

Serotonin Modulators
- Nefazodone
- Trazodone
- Vilazodone[e)]
- Vortioxetine[e)]

Selective Serotonin Reuptake Inhibitors (SSRIs)
- Citalopram
- Escitalopram
- Fluoxetine
- Fluvoxamine
- Paroxetine[b)]
- Sertraline

Monoamine Oxidase Inhibitors (MAOIs)
- Isocarboxazid
- Phenelzine
- Tranylcypromine
- Rasagiline[c)]
- Selegiline[c)]

Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)
- Desvenlafaxine
- Duloxetine
- Levomilnacipran[e)]
- Venlafaxine
- Milnacipran[d)]

Miscellaneous
- Bupropion
- Mirtazapine

Note: a) denotes tertiary TCAs; b) denotes drugs with strong anticholinergic properties; c) denotes a MAO-B inhibitor and is primarily classified as anti-Parkinsonian agents; d) is primarily classified as fibromyalgia agents; e) indicates that it is not available in NAMCS; and f) indicates that it should be avoided, regardless of diagnosis, according to 2012 Beers criteria.

Appendix 4.3. 2012/2015 Beers criteria for potentially inappropriate antidepressant use in older adults due to drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome

Disease or syndrome (ICD-9-CM code)	Antidepressant[a)]	Rationale	Recommendation	Quality of Evidence	Strength of recommendation
Cardiovascular					
Syncope (780.2, 992.1)	Tertiary TCAs	Increase risk of orthostatic hypotension or bradycardia	Avoid	Moderate	Strong
Central nervous system					
Chronic seizures or epilepsy (345, 780.33)	bupropion; maprotiline	Lowers seizure threshold; may be acceptable in patients with well-controlled seizures in whom alternative agents have not been effective	Avoid	Moderate	Strong
Delirium (290.11, 290.3, 290.41, 291.0, 292.81, 293.0, 293.1)	TCAs; Anticholinergics	Induce or worsen delirium in older adults; if discontinuing drugs used chronically, taper to avoid withdrawal symptoms	Avoid	Moderate	Strong
Dementia and cognitive impairment (290, 291.2, 292.82, 294.10, 294.11, 294.20, 294.21, 331.0, 331.19, 331.82, 331.83)	Anticholinergics	Avoid because of adverse CNS effects	Avoid	High	Strong
History of falls or fractures (E880-E888)	TCAs; SSRIs	Ability to produce ataxia, impaired psychomotor function, syncope, and additional falls	Avoid unless safer alternatives are not available	High	Strong
Gastrointestinal					
Chronic constipation (564)	Tertiary TCAs; Anticholinergics	Can worsen constipation	Avoid unless no other alternatives	Moderate to low	Weak
Lower urinary tract symptoms, benign prostatic hyperplasia (600)	Anticholinergics	May decrease urinary flow and cause urinary retention	Avoid in men	Moderate	Inhaled agents: strong; others: weak

Note: a) refers to appendix 4.1 for full description.

CHAPTER 5

Manuscript #3: Effects of Depression Screening on Diagnosing and Treating Mood Disorders among Older Adults in Office-based Primary Care Outpatient Settings: An Instrumental Variable Analysis

Keywords: depression screening, depression, mood disorders, antidepressant, aged, primary care

Abstract text word count: 233 (≤ 250)
Article text word count: 3,073 (≤ 3,500)
Number of tables: 4
Number of figures: 1
Number of appendices: 3

Joint Acknowledgment/Disclosure Statement: Dr. Rhee conceived the study, acquired data, analyzed and interpreted the data, led the writing of the manuscript, and oversaw every aspect of the study. Drs. Capistrant, Schommer, Hadsall and Uden contributed to revising the manuscript.

Funding Source: As part of authors' regular salary and fringe benefits, different departments from the University of Minnesota provided financial support for this study. This funding arrangement ensured the authors' independence in writing and publishing this original research.

Conflict of Interest: The authors declare that they do not have a conflict of interest.

Disclaimers: Publicly available data were obtained from the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC). Analyses, interpretation, and conclusions are solely those of the authors and do not necessarily reflect the views of the Division of Health Interview Statistics or NCHS of the CDC.

Compliance with Ethical Standards: Using publicly available de-identified data, the research procedure for this study was exempted from the University of Minnesota Institutional Review Board.

ABSTRACT

Existing literature shows mixed findings regarding the efficacy and effectiveness of depression screening, and relatively little is known about the effectiveness of depression screening among older adults in primary care visits in the U.S. This study examines the effects of depression screening on the three following outcomes: mood disorder diagnoses, overall antidepressant prescriptions, and potentially inappropriate antidepressant prescriptions among older adults ages 65 or older in office-based outpatient primary care settings. We used data from 2010-2012 National Ambulatory Medical Care Survey (NAMCS), a nationally representative sample of office-based primary care outpatient visits among older adults (n=9,313 unweighted). We employed an instrumental variable approach to control for selection bias in our repeated cross-sectional population-based study. Injury prevention and stress management were selected as instrumental variables, as they were considered completely exogenous to outcomes of interests using conceptual and statistical criteria. We conducted multivariate bivariate probit (*biprobit*) regression analyses to investigate the effect of depression screening on each outcome, when controlled for other covariates. We found that depression screening was negatively associated with potentially inappropriate antidepressant prescriptions (b=-2.17; 95% CI -2.80 – -1.53; $p<0.001$). However, no significant effect of depression screening on diagnosis of mood disorders and overall antidepressant prescriptions was found. Overall, depression screening had a negative effect on potentially inappropriate antidepressant prescriptions. Primary care physicians and other healthcare providers should actively utilize depression screening to minimize potentially inappropriate antidepressant prescriptions in older adult patients.

Word Count: 233 (out of 250)

5.1 Introduction

Since the mid-1990s, depression screening has been a "prominent component of the "detect—treat—improve" paradigm for undetected depression" in primary care settings.[1(p.280)] While community-dwelling ambulatory adults with depression are not likely to visit a psychiatrist for their depression or other mood disorders, they still seek care in primary care or other specialty visits, making "these visits particularly important opportunities to detect and initiate treatment of depression" or other mood disorders.[1(p. 279)] In the U.S., the rate of providing depression screening in primary care and other specialty visits remains relatively low; a recent study using national data suggests that approximately 5% of all visits had depression screening among adults ages 18 or over in 2006-2010.[2]

Since late 1990s, the U.S. Preventive Services Task Force (USPSTF), as part of the Agency for Healthcare Research and Quality (AHRQ), have put significant efforts to creating and disseminating depression screening guidelines.[3] In 2002, the USPSTF recommended depression screening for all eligible adults (i.e., a grade B recommendation), indicating that clinicians should routinely screen for depression because there is at least fair evidence of depression screening that "improves important health outcomes and [such] benefits outweigh harms."[3(p. 763)] Such a key recommendation has remained stable in updated USPSTF statements over time in 2009 and 2016.[4,5]

Despite clinical and policy efforts, the utility of depression screening is controversial in existing literature. As summarized in Mojtabai's work,[6] advocates of depression screening highlight that depression screening should be used as the rates of detection and treatment of depression are relatively low given that the prevalence of

depression and other mood disorders remains high among ambulatory adults. Critics, on the other hand, suggest that false-positive rates of depression screening are high, such that depression screening is not a cost-effective approach.[6-11] While existing evidence supports promising efficacy of depression screening in primary care settings, most of these studies were randomized controlled trials (RCTs) or systematics reviews from these RCTs.[7,10]

Unlike RCTs, which emphasize efficacy in ideal settings, population-based observational studies can evaluate the effectiveness of depression screening with greater validity in real-world settings.[12] To our knowledge, only one observational study had been conducted to describe the effect of depression screening on diagnosing and treating mood disorders.[6] The study suggests that depression screening was negatively associated with antidepressant prescriptions without a diagnosis of mood disorder.[6] The study, however, focused on the general U.S. population, and did not address potentially inappropriate antidepressant prescriptions in older adult populations.[6]

In the U.S., an inventory of potentially inappropriate medications for older adults was created by Beers and his colleagues (hereafter referred to as Beers criteria) in the early 1990s,[13] and the Beers criteria has been updated over time.[14,15] Using the updated Beers criteria, a recent study estimated that 30.9% of older adults are exposed to potentially inappropriate medications.[16] This is a public health issue that impacts potentially avoidable healthcare expenditures,[17-19] increased hospitalization,[20-24] morbidity[25] and mortality[23] rates. In light of clinical efforts to minimize potentially inappropriate prescriptions, we hypothesize that depression screening may help avoid the prescribing of potentially inappropriate antidepressant medications in older adults. To

address these gaps, our study examines whether or not depression screening has potential effects on diagnosing and treating mood disorders among older adults who made office-based primary care outpatient visits.

5.2 Methods

Data Source and Study Sample

We used data from 2010-2012 National Ambulatory Medical Care Survey (NAMCS) (n=138,431 unweighted), which is administrated by National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC),[26] The NAMCS is an annual cross-sectional survey of visits to office-based physicians in outpatient settings, and provides reliable information about the provision and/or use of ambulatory medical care services in the United States.[26] Our final analytic sample included older adults ages 65 and over, who had primary care visits, and had completed data for all covariates (n=9,313 unweighted). Exclusion criteria were individuals ages 64 or younger (n=100,314 unweighted), and had visits other than primary care visits (i.e., specialty visits) (n=28,105 unweighted). This study was deemed exempt by the University of Minnesota Institutional Review Board, as we used publicly available de-identified data. Further details of the survey, including descriptions, questionnaires, sampling methodology and datasets, are publicly available on the NAMCS website.[27]

Measures

Dependent variables. Three main outcomes of interests were: diagnosis of mood disorders, antidepressant prescriptions, and potentially inappropriate antidepressant

prescriptions. First, we included the diagnosis of mood disorders (e.g., major depression, bipolar disorders, and other affective disorders) (see Appendix 5.1).[28] The NAMCS collects up to three clinical diagnoses using the *International Classification of Diseases, 9th edition, clinical modification* (ICD-9-CM), and a binary variable (yes or no/missing) was constructed for the diagnosis of mood disorders (see Appendix 5.1).

For antidepressant prescriptions as an outcome measure, the NAMCS collects up to eight medications in 2010-2011, and up to 10 medications in 2012. For consistency across data, we only included the first eight medications. Using the *2015 American Hospital Formulary Service (AHFS) Compendium*,[29] Wolters Kluwer's *Drug Facts and Comparisons*,[30] and previous studies,[31-36] we identified prescription-based antidepressant medications using generic names (see Appendix 5.2). We constructed a binary variable (yes or no) for overall antidepressant prescriptions. For potentially inappropriate antidepressant prescriptions, we constructed a binary variable (yes or no) using the 2012/2015 Beers Criteria (see Appendices 5.2 and 5.3).[14,15]

Independent variable. The key independent variable in this study was depression screening status (yes or no). The NAMCS specifically asks the following question, "Was the depression screening exam ordered or provided at the visit?"

Instrumental variables. We included two instrumental variables, injury prevention and stress management. The NAMCS asks, "Was health education related to [injury prevention or stress management] ordered or provided at the visit?" These instrumental variables were binary (yes or no) in nature. The selection of these instrumental variables

was based on both conceptual and statistical criteria. Conceptually, the selected instrumental variables reflect either "the physician's greater opportunities to assess and to counsel on preventive health issues"[6(p.466)] or "[indication of] working in practice settings that encourage or require more detailed and extensive preventive interventions and patient education."[6(p. 466)] In such cases, provision of health education related to injury prevention and/or stress management seems highly correlated with depression screening as part of preventive care. It is also argued that injury prevention and/or stress management are completely exogenous to outcomes of interests because such preventive care may lead to better diagnoses of mental health conditions and/or appropriate use of antidepressants. Statistically, using bivariate analyses, these instrumental variables were adequate as they were significantly associated with the depression screening, but not with the outcomes of interests ($p<0.05$).

Control variables. Based on previous studies,[31,34,35,37-45] we included a number of covariates. For demographics, we included: age (65-74, 75-84, or 85+), gender, race/ethnicity, census region, primary source of payment (Medicare, Medicaid, private, or others), reason for visit (acute problem, routine chronic problem, preventive care, or pre-/post-surgery care), and repeat of visits within the past 12 months (none, 1-2, 3-5, or 6+). We included the following clinical characteristics: type of medical practice (solo or others), metropolitan statistical area (MSA) status, which describes high population density (yes for "one or more counties that contain a city of 50,000 or more inhabitants, or contain a Census Bureau-defined urbanized area and have a total population of at least 100,000 (75,000 in New England)" or no for otherwise),[46] time spent with doctor (<15,

15-20, 21-30, or >30 min.), number of chronic conditions (none, 1, 2-3, or 4+),[47] and number of medications (0-2, 3-5, or 6+). We also included non-pharmacological psychiatric service use (yes or no), as the NAMCS asks two questions whether psychotherapy and mental health counseling other than psychotherapy were provided or ordered at the visit. The variable, repeat of visits in the past 12 months, had the largest missing proportion (31.9%), and was imputed based on age, gender and the number of medications using the *hotdeck* imputation technique.[48] Other variables that had missing values were: primary source of payment (4.3%), reason for visit (1.3%), and the number of chronic conditions (1.2%). Observations with all of these missing values (n=699 unweighted) were systematically excluded, leaving the final sample size of 9,313 visits (unweighted).

Data Analysis

First, we examined the extent to which demographic and clinical characteristics differed by depression screening status in older adults. We used design-based *F*-tests to investigate such differences. We also estimated the prevalence of mood disorder diagnoses and antidepressant prescriptions by depression screening in our analytic sample.

Second, we conducted two different regression analyses: naïve probit and bivariate probit (*biprobit*) models, for each outcome of interests.[6,49] In naïve probit models, the issue of endogeneity of depression screening (i.e., selection bias) was ignored such that we regressed each outcome on depression screening while controlled for covariates. Each *biprobit* model, on the other hand, comprises of two-part models that adjusts for endogeneity issue of depression screening. In each *biprobit* model, the first

part has depression screening as an outcome variable, and regressed it on two instrumental variables, while controlling for other covariates. Then, in the second part model, we regressed each outcome of interests on the first part of the model, while controlling for covariates, respectively. The *biprobit* models approach was considered appropriate after testing for issues related to endogeneity and overidentification. After running the *biprobit* models, we only interpreted the final models (i.e., after second part) as the interpretations are similar to those of naïve probit models. This makes interpretations comparable where naïve probit models ignored the endogeneity issue (i.e., selection bias), and *biprobit* models adjusted for endogeneity and overidentification issues. Stata 13.1[50] was used for all analyses and the *svy* commands in Stata were employed to account for the complex sample design of the NAMCS (i.e., unequal probability of selection, clustering and stratification).

5.3 Results

Characteristics of the Study Sample

Table 5.1 shows demographic and clinical characteristics of older adults in office-based primary care outpatient settings by the depression screening status. In demographic characteristics, reason for visits and MSA status were significantly different by the depression screening status. For example, 76.2% of those with screened visits had routine chronic problems or preventive care as primary reasons for visits, which was significantly higher than that of non-screened visits (65.7%) (p=0.023). 90.2% of those with screened visits were located in MSAs, whereas 79.5% of non-screened visits were located in MSAs (p=0.009).

We found significant differences in all clinical characteristics. For instance, 86.7% of screened visits involved two or more multiple chronic conditions, which was significantly higher than that of non-screened visits (71.0%) (p<0.001). Similarly, 76.8% of screened visits had three or more medications prescribed, which was significantly higher than that of non-screened visits (67.5%) (p=0.038). Non-pharmacological psychiatric services were more commonly provided in screened visits (11.1%) than those in non-screened visits (0.5%) (p<0.001). Similarly, health education related to injury prevention and stress management were more commonly provided in screened visits than those in non-screen visits (p<0.001).

<Table 5.1 about here>

Depression screening was conducted in 209 out of 9,313 visits (unweighted) by primary care office-based physicians. As shown in both Table 5.1 and Figure 5.1, diagnosis of mood disorders and antidepressant prescriptions were significantly differed by depression screening (p<0.001). For example, 15.5% of visits with depression screening had both mood disorders diagnosed and antidepressants prescribed, which was at least five times larger than those in visits without depression screening. Furthermore, 26.3% of visits with depression screening had either mood disorders diagnosed or antidepressants, and this was almost twofold higher than that of visits without depression screening (p<0.001). Overall, higher rates of diagnosis of mood disorders and antidepressant prescriptions were observed in visits with depression screening, when compared to visits without depression screening.

<Figure 5.1 about here>

Multivariate naïve and probit analyses

Table 5.2 presents naïve and *biprobit* models with diagnosis of mood disorders as the primary outcome of interest. In the naïve probit model, depression screening was positively associated with the diagnosis of mood disorders when controlled for other covariates (b=0.69; 95% CI 0.41–0.98; $p<0.001$). In the *biprobit* model, depression screening was significantly associated with two instrumental variables, injury prevention and stress management, ($p=0.002$, respectively) in the first part model. When this first part model was applied in the second part model, depression screening was no longer significantly associated with the diagnosis of mood disorders while the relationship was still positive (b=1.08; 95% CI -0.13–2.30; $p=0.080$).

<Table 5.2 about here>

Table 5.3 shows naïve and *biprobit* models, where the variable, antidepressant prescriptions, was the primary outcome of interest. The diagnosis of mood disorders was controlled for among other covariates. Depression screening was positively associated with the antidepressant prescriptions, holding other variables constant, in the naïve probit model (b=0.37; 95% CI 0.09–0.64; $p=0.010$). In the first part model of the *biprobit* model, depression screening was positively associated with both instrumental variables, injury prevention and stress management ($p=0.005$ and $p=0.002$, respectively). When this first part model was applied to the second part model in the *biprobit* model, depression screening was no longer significantly associated with the antidepressant prescriptions, while magnitude was even larger and the relationship was still positive (b=0.96; 95% CI -0.59–2.51; $p=0.225$).

<Table 5.3 about here>

Table 5.4 presents naïve and *biprobit* models with the outcome of potentially inappropriate antidepressant prescriptions. Other covariates, including the diagnosis of mood disorders, were controlled for in both models. Unlike previous models (see Tables 5.2 and 5.3), depression screening was negatively associated with the potentially inappropriate antidepressant prescriptions in the naïve probit model (b=-0.95; 95% CI -1.46 – -0.44; $p<0.001$). In the first part model of the *biprobit* models, depression screening was positively associated with two instrumental variables, injury prevention and stress management ($p=0.005$ and $p=0.001$, respectively), which are consistent with previous models (see Tables 5.2 and 5.3). When this first part model was applied in the second part model of the *biprobit* model, depression screening was negatively associated with the potentially inappropriate antidepressant prescriptions (b=-2.17; 95% CI -2.80 – -1.53; $p<0.001$).

<Table 5.4 about here>

5.4 Discussion

This is the first population-based observation study to investigate effects of depression screening on diagnosis of mood disorders, overall antidepressant prescriptions, and potentially inappropriate antidepressant prescriptions among older adults in office-based primary care outpatient visits, using an instrumental variable approach. When controlling for a 2009 USPSTF depression screening guideline recommendation,[51] our study suggests that no effect of depression screening on diagnosis of mood disorders and overall antidepressant prescriptions was found. However, a negative effect of depression screening on potentially inappropriate antidepressant prescriptions was found.

First, using naïve probit models, depression screening was positively associated with diagnosis of mood disorders and overall antidepressant prescriptions. The significance of positive associations in these models disappeared when the instrumental variable approach was applied. Furthermore, the significance of clinical characteristics that had differed by depression screening using the naïve probit model disappeared in the *biprobit* models. Such findings and patterns are consistent with a previous study.[6] Our findings, however, are in contrast with several RCT studies, which showed promising evidence of the role of depression screening in these outcomes.[6,7,52] As suggested by Mojtabai,[6] depression and other mood disorders detected by depression screening may be less severe, such that physicians and other healthcare providers (e.g., physician assistants) may be less likely to diagnose and treat depression and other mood disorders, when using the depression screening measures alone.[7] An alternative explanation is that in RCT studies, certain depression screening tools were systematically used and tested for their efficacy under ideal settings. In the real world, no specific depression screening tool has been specifically recommended for this population of interest.[53] If primary care physicians and other healthcare providers are not well-informed about depression screening tools and their utilities, they may not likely diagnose and treat depression and other mood disorders. Future research should elucidate discrepancies in findings from RCTs and population-based observational studies.

Second, using both naïve probit model and *biprobit* model, depression screening was negatively associated with potentially inappropriate antidepressant prescriptions, implying that depression screening is effective in reducing potentially inappropriate antidepressant prescriptions. Considering that visits with depression screening—

compared to those without depression screening—had higher rates of diagnosis of mood disorders and overall antidepressant prescriptions (see Figure 5.1), physicians and other healthcare providers who use depression screening may also be more sensitive to clinical guidelines, such as Beers Criteria,[15] to minimize potentially inappropriate medications. Future research should address this speculation to better understand the potential role of depression screening on potentially inappropriate antidepressant prescriptions.

Our findings have several policy and clinical implications. First, considering that the rate of antidepressant prescriptions has dramatically increased in the past decade,[54] there are increasing concerns about potentially inappropriate antidepressant use. For example, one study indicates that approximately one in 10 antidepressant-related visits, regardless of physician specialties, is exposed to potentially inappropriate antidepressant prescriptions in older adults. Another study[51] revealed that the 2009 USPSTF depression screening recommendation resulted in no impact on prescribing patterns of antidepressants. Our study, however, suggests that depression screening still plays a significant, negative role on potentially inappropriate antidepressant prescriptions in older adults, and it may not be due to policy initiatives. Because our study advocates that depression screening works to reduce potentially inappropriate antidepressant prescriptions in older adults, policymakers should promote the use of depression screening in this population with potential revision of the guideline to boost its utility. For clinical practice, while practice modifications with respect to depression screening would require further research in the near future, primary care physicians and other healthcare providers should actively follow the depression screening guideline along with

their judgement calls to provide the best available healthcare to older adult patients in their visits.

This study has several limitations. First, the NAMCS data capture up to three diagnoses only in a sampled visit. Given these limited diagnoses, and considering that older adults often have multiple chronic conditions (see Table 5.1), it may have underreported potentially inappropriate antidepressant prescriptions due to drug-disease or drug-syndrome interactions.[54] Second, in a given sampled visit with cross-sectional nature of survey design, the course and outcome of treatments (e.g., long-term use of antidepressants) cannot be assessed.[6] In addition, refills of antidepressant medications without mental health diagnoses at each visit might have not been captured. Such issues might have led to underreporting of mental health diagnoses and potentially inappropriate antidepressant prescriptions. Findings from this study should be interpreted with these potential limitations.

Overall, this study reveals evidence that depression screening is effective in reducing potentially inappropriate antidepressant prescriptions among older adults in office-based primary care outpatient visits. Future research should address the reasons and rationales for such effect of depression screening.

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Figure 5.1. Prevalence of antidepressant prescriptions and mood disorder diagnoses among older adults in office-based primary care outpatient settings, 2010-2012 NAMCS.

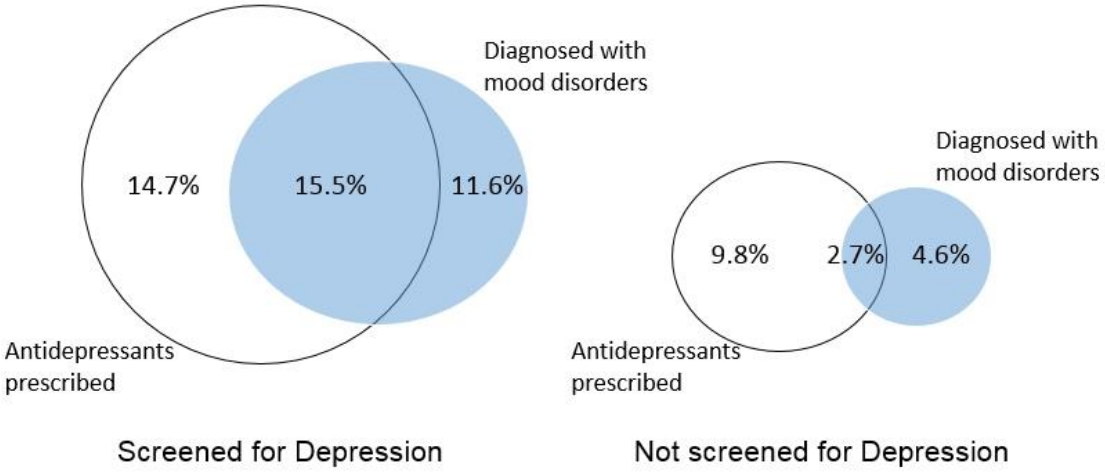

Table 5.1. Selected baseline characteristics (weighted percent) of older adults in office-based primary care outpatient settings by depression screening, 2010-2012 NAMCS.

	Depression screening		Total	*P*-value
	No	Yes		
Sample size				
Unweighted sample	9,104	209	9,313	
Weighted population	91,278,108	1,727,366	93,005,474	
Age				
65-74	50.5	50.4	50.5	0.9633
75-84	35.0	36.0	35.0	
85+	14.5	13.7	14.5	
Gender				
Female	56.6	61.0	56.7	0.4471
Male	43.4	39.0	43.3	
Race/ethnicity				
Non-Hispanic White	78.3	71.6	78.2	0.1571
Non-Hispanic Black	8.5	13.0	8.6	
Hispanic	8.3	14.2	8.4	
Others[a)]	5.0	1.2	4.9	
Region				
Northeast	18.7	12.7	18.6	0.0566
Midwest	21.8	12.0	21.7	
South	35.5	48.3	35.7	
West	24.0	27.0	24.0	
Source of payment				
Private	14.7	14.1	14.7	0.7435
Medicare	82.4	84.0	82.4	
Medicaid	1.6	0.8	1.6	
Others[b)]	1.3	1.1	1.3	
Reason for visit				
Acute problem	31.4	22.8	31.3	0.0229
Routine chronic problem	49.3	47.5	49.3	
Preventive care	16.4	28.7	16.6	
Pre- or post-surgery	2.9	1.0	2.9	
Repeat of visits				
0 visit	6.6	6.9	6.6	0.5784
1-2 visits	31.0	36.8	31.1	
3-5 visits	35.2	30.3	35.2	
6+ visits	27.2	25.9	27.1	
Type of medical practice				
Solo	89.6	87.8	89.5	0.6558
Others[c)]	10.4	12.2	10.5	
MSA status				
MSA	79.5	90.2	79.7	0.0089
Non-MSA	20.5	9.8	20.3	

Time spent with doctor				
< 15 min.	14.0	12.0	14.0	
15-20 min.	52.2	41.1	52.0	0.0562
21-30 min.	21.8	30.3	22.0	
> 30 min.	12.0	16.6	12.1	
Multiple chronic conditions (MCCs)				
None	8.9	2.7	8.8	
1	20.1	10.6	19.9	<0.0001
2-3	47.2	43.1	47.2	
4+	23.8	43.6	24.1	
Number of medications				
0	11.3	3.1	11.1	
1-2	21.2	20.1	21.2	0.0381
3-5	25.9	24.0	25.8	
6+	41.6	52.8	41.9	
Mood disorder diagnosis[d)]				
None/missing	92.7	72.9	92.4	
Major depression	0.2	2.3	0.2	
Dysthymia	0.4	2.7	0.4	<0.0001
Bipolar disorder	0.1	1.6	0.1	
Other affective disorder	1.6	12.7	1.8	
Others	5.0	7.8	5.1	
Antidepressant prescription				
No	87.6	69.8	87.2	
Yes, appropriate	11.0	30.1	11.4	<0.0001
Yes, potentially inappropriate	1.5	0.1	1.4	
Non-pharmacological psychiatric services				
Yes	0.5	11.1	0.7	<0.0001
No	99.5	88.9	99.3	
Injury prevention				
Yes	1.9	7.8	2.0	0.0004
No	98.1	92.2	98.0	
Stress management				
Yes	1.6	16.1	1.8	<0.0001
No	98.5	83.9	98.2	

Note: a) includes Asians, American Indian/Alaska Natives (AIANs), Native Hawaiian or Other Pacific Islanders (NHOPI), and multiple races; b) includes worker's compensation, self-pay, no charge, and others; c) includes federally qualified health center (FQHC), non-federal government clinic, family planning clinic, health maintenance organization (HMO) or other prepaid practice plan, and faculty practice plan; and d) refers to appendix 5.1.

Table 5.2. Naïve and bivariate probit analyses for diagnosis of mood disorders among older adults in office-based primary outpatient care settings, NAMCS 2010-2012.

	Naïve probit model for diagnosis of mood disorders			Bivariate probit model					
				Model for depression screening			Model for diagnosis of mood disorders[d)]		
Variables (Reference group in parenthesis)	b	95% CI	*P*-value	b	95% CI	*P*-value	b	95% CI	*P*-value
Depression screening (No)									
Yes	**0.69**	**0.41 - 0.98**	**<0.001**	**-**	**-**	**-**	**1.08**	**-0.13 - 2.30**	**0.080**
Age (65-74)									
75-84	0.14	0.02 - 0.27	0.023	0.04	-0.13 - 0.22	0.643	0.14	0.02 - 0.26	0.024
85+	0.51	0.36 - 0.66	<0.001	-0.04	-0.31 - 0.23	0.779	0.51	0.36 - 0.66	<0.001
Gender (Male)									
Female	0.22	0.10 - 0.33	<0.001	0.08	-0.10 - 0.25	0.390	0.22	0.11 - 0.33	<0.001
Race/ethnicity (Non-Hispanic White)									
Non-Hispanic Black	-0.07	-0.28 - 0.15	0.557	0.12	-0.30 - 0.54	0.579	-0.07	-0.29 - 0.15	0.539
Hispanic	-0.06	-0.26 - 0.15	0.584	0.15	-0.21 - 0.52	0.418	-0.06	-0.26 - 0.15	0.887
Others[a)]	-0.24	-0.56 - 0.08	0.146	-0.41	-0.88 - 0.05	0.083	-0.23	-0.55 - 0.09	0.153
Region (Northeast)									
Midwest	0.07	-0.12 - 0.26	0.46	0.08	-0.24 - 0.39	0.635	0.07	-0.12 - 0.26	0.454
South	0.16	-0.02 - 0.33	0.085	0.41	0.11 - 0.71	0.007	0.15	-0.03 - 0.33	0.096
West	0.18	-0.01 - 0.36	0.063	0.26	-0.08 - 0.61	0.134	0.17	-0.01 - 0.36	0.066
Source of payment (Medicare)									
Private	-0.04	-0.19 - 0.11	0.588	-0.11	-0.40 - 0.18	0.471	-0.04	-0.18 - 0.11	0.608
Medicaid	0.51	0.11 - 0.90	0.011	-0.32	-0.95 - 0.31	0.317	0.51	0.12 - 0.90	0.011
Others[b)]	0.04	-0.23 - 0.32	0.751	-0.50	-1.19 - 0.20	0.162	0.05	-0.23 - 0.32	0.737
Reason for visit (Acute problem)									
Routine chronic problem	0.22	0.09 - 0.35	0.001	0.05	-0.18 - 0.29	0.663	0.22	0.09 - 0.35	0.001
Preventive care	0.04	-0.13 - 0.20	0.642	-0.54	-1.24 - 0.15	0.125	-0.05	-0.46 - 0.35	0.794
Pre- or post-surgery	-0.06	-0.46 - 0.35	0.788	0.33	0.05 - 0.62	0.022	0.03	-0.14 - 0.20	0.709
Repeat of visits (None)									
1-2 visits	0.26	0.01 - 0.50	0.042	-0.19	-0.49 - 0.12	0.229	0.26	0.01 - 0.51	0.039
3-5 visits	0.18	-0.07 - 0.43	0.159	-0.15	-0.40 - 0.11	0.264	0.18	-0.07 - 0.43	0.148
6+ visits	0.24	0.00 - 0.49	0.049	-0.34	-0.66 - -0.02	0.038	0.25	0.01 - 0.49	0.044
Type of medical practice (Solo)									
Others[c)]	-0.09	-0.35 - 0.16	0.476	0.15	-0.19 - 0.48	0.383	-0.09	-0.35 - 0.16	0.462

MSA status (MSA)									
Non-MSA	0.09	-0.09 - 0.27	0.319	-0.39	-0.67 - -0.10	0.007	0.09	-0.08 - 0.27	0.289
Time spent with doctor (< 15 min.)									
15-20 min.	0.13	-0.05 - 0.32	0.160	-0.12	-0.36 - 0.13	0.344	0.13	-0.05 - 0.32	0.152
21-30 min.	0.19	0.02 - 0.35	0.031	0.09	-0.11 - 0.29	0.359	0.18	0.01 - 0.35	0.033
> 30 min.	0.20	0.01 - 0.40	0.045	0.10	-0.18 - 0.38	0.488	0.20	0.00 - 0.40	0.045
Multiple chronic conditions (MCCs)									
(None)									
1	0.01	-0.20 - 0.23	0.899	0.17	-0.30 - 0.64	0.486	0.12	-0.21 - 0.22	0.912
2-3	0.05	-0.17 - 0.27	0.638	0.37	-0.10 - 0.83	0.123	0.05	-0.17 - 0.27	0.661
4+	0.04	-0.20 - 0.28	0.742	0.65	0.17 - 1.12	0.008	0.03	-0.21 - 0.27	0.812
Number of medications (None)									
1-2	0.10	-0.07 - 0.28	0.245	0.49	0.09 - 0.89	0.017	0.10	-0.08 - 0.27	0.272
3-5	-0.01	-0.21 - 0.20	0.956	0.45	0.07 - 0.83	0.020	-0.01	-0.22 - 0.20	0.924
6+	0.11	-0.05 - 0.27	0.190	0.51	0.11 - 0.90	0.012	0.10	-0.06 - 0.27	0.214
Psychiatric services (No)									
Yes	1.50	1.08 - 1.92	<0.001	1.26	0.65 - 1.87	<0.001	1.4	0.86 - 1.94	<0.001
Injury prevention (No)									
Yes	-	-	-	**0.64**	**0.23 - 1.05**	**0.002**	-	-	-
Stress management (No)									
Yes	-	-	-	**0.85**	**0.32 - 1.38**	**0.002**	-	-	-

Note: rho = 0.30; p<0.001. a) includes Asians, American Indian/Alaska Natives (AIANs), Native Hawaiian or Other Pacific Islanders (NHOPI), and multiple races; b) includes worker's compensation, self-pay, no charge, and others; c) includes federally qualified health center (FQHC), non-federal government clinic, family planning clinic, health maintenance organization (HMO) or other prepaid practice plan, and faculty practice plan; and d) refers to appendix 5.1.

Table 5.3. Naïve and bivariate probit analyses for antidepressant prescriptions among older adults in office-based primary care outpatient settings, NAMCS 2010-2012.

	Naïve probit model for antidepressant prescriptions			Bivariate probit model					
				Model for depression screening			Model for antidepressant prescriptions		
Variables (Reference group in parenthesis)	b	95% CI	*P*-value	b	95% CI	*P*-value	b	95% CI	*P*-value
Depression screening (No)									
Yes	**0.37**	**0.09 - 0.64**	**0.010**	**-**	**-**	**-**	**0.96**	**-0.59 - 2.51**	**0.225**
Diagnosis of mood disorders[a)] (No/missing)									
Yes	0.96	0.79 - 1.13	<0.001	0.52	0.29 - 0.76	<0.001	0.94	0.75 - 1.12	<0.001
Age (65-74)									
75-84	-0.09	-0.20 - 0.02	0.095	0.03	-0.14 - 0.21	0.711	-0.09	-0.20 - 0.02	0.099
85+	-0.11	-0.28 - 0.05	0.177	-0.09	-0.37 - 0.18	0.507	-0.11	-0.28 - 0.06	0.191
Gender (Male)									
Female	0.21	0.10 - 0.33	<0.001	0.04	-0.14 - 0.21	0.687	0.21	0.10 - 0.33	<0.001
Race/ethnicity (Non-Hispanic White)									
Non-Hispanic Black	-0.43	-0.65 - -0.20	<0.001	0.17	-0.23 - 0.58	0.407	-0.43	-0.66 - -0.20	<0.001
Hispanic	-0.19	-0.35 - -0.02	0.027	0.14	-0.24 - 0.51	0.474	-0.19	-0.36 - -0.02	0.029
Others[b)]	-0.24	-0.66 - 0.19	0.272	-0.45	-0.89 - -0.00	0.049	-0.23	-0.65 - 0.19	0.287
Region (Northeast)									
Midwest	-0.12	-0.27 - 0.03	0.125	-0.05	-0.27 - 0.36	0.757	-0.12	-0.27 - 0.03	0.128
South	0.07	-0.08 - 0.22	0.345	0.40	0.11 - 0.70	0.008	0.06	-0.09 - 0.21	0.400
West	0.03	-0.15 - 0.20	0.752	0.25	-0.11 - 0.60	0.173	0.02	-0.15 - 0.20	0.793
Source of payment (Medicare)									
Private	0.09	-0.05 - 0.23	0.218	-0.08	-0.39 - 0.23	0.616	0.09	-0.05 - 0.23	0.205
Medicaid	0.18	-0.07 - 0.43	0.153	-0.31	-0.98 - 0.37	0.374	0.19	-0.06 - 0.44	0.134
Others[c)]	-0.00	-0.36 - 0.35	0.996	-0.30	-0.83 - 0.22	0.255	-0.01	-0.35 - 0.36	0.973
Reason for visit (Acute problem)									
Routine chronic problem	-0.01	-0.13 - 0.10	0.820	0.07	-0.17 - 0.30	0.567	-0.01	-0.13 - 0.10	0.814
Preventive care	-0.08	-0.21 - 0.05	0.247	0.37	0.10 - 0.64	0.007	0.23	-0.13 - 0.60	0.214
Pre- or post-surgery	0.23	-0.13 - 0.59	0.214	-0.70	-1.53 - 0.14	0.103	-0.09	-0.22 - 0.04	0.188
Repeat of visits (None)									
1-2 visits	-0.04	-0.27 - 0.19	0.731	-0.21	-0.54 - 0.12	0.208	-0.03	-0.26 - 0.19	0.791
3-5 visits	0.02	-0.22 - 0.25	0.884	-0.18	-0.47 - 0.11	0.216	0.02	-0.20 - 0.25	0.832
6+ visits	0.13	-0.11 - 0.37	0.280	-0.42	-0.78 - -0.06	0.023	0.14	-0.09 - 0.37	0.229

Type of medical practice (Solo)									
Others[d)]	0.07	-0.15 - 0.29	0.552	0.14	-0.18 - 0.46	0.394	0.06	-0.16 - 0.28	0.567
MSA status (MSA)									
Non-MSA	-0.06	-0.20 - 0.07	0.351	-0.40	-0.70 - -0.11	0.007	-0.06	-0.19 - 0.08	0.412
Time spent with doctor (< 15 min.)									
15-20 min.	-0.00	-0.14 - 0.15	0.948	-0.10	-0.35 - 0.14	0.397	0.01	-0.14 - 0.15	0.905
21-30 min.	0.10	-0.06 - 0.27	0.202	0.09	-0.12 - 0.30	0.401	0.10	-0.06 - 0.26	0.213
> 30 min.	0.03	-0.17 - 0.22	0.784	0.08	-0.22 - 0.39	0.580	0.02	-0.17 - 0.21	0.808
Multiple chronic conditions (MCCs) (None)									
1	-0.02	-0.24 - 0.21	0.869	0.19	-0.25 - 0.64	0.392	-0.02	-0.25 - 0.20	0.855
2-3	-0.12	-0.35 - 0.10	0.284	0.38	-0.07 - 0.83	0.099	-0.13	-0.35 - 0.10	0.266
4+	-0.02	-0.25 - 0.21	0.861	0.66	0.20 - 1.11	0.005	-0.04	-0.26 - 0.19	0.761
Number of medications (0-2)									
3-5	0.78	0.60 - 0.95	<0.001	0.07	-0.19 - 0.33	0.602	0.77	0.60 - 0.95	<0.001
6+	1.35	1.19 - 1.52	<0.001	0.12	-0.11 - 0.36	0.303	1.34	1.18 - 1.51	<0.001
Psychiatric services (No)									
Yes	0.49	0.02 - 0.96	0.042	1.07	0.46 - 1.69	0.001	0.34	-0.30 - 0.97	0.299
Injury prevention (No)									
Yes	-	-	-	**0.61**	**0.18 - 1.03**	**0.005**	-	-	-
Stress management (No)									
Yes	-	-	-	**0.77**	**0.27 - 1.27**	**0.002**	-	-	-

Note: rho = 0.14; p=0.007. a) refers to appendix 5.1; b)includes Asians, American Indian/Alaska Natives (AIANs), Native Hawaiian or Other Pacific Islanders (NHOPI), and multiple races; c) includes worker's compensation, self-pay, no charge, and others; and d) includes federally qualified health center (FQHC), non-federal government clinic, family planning clinic, health maintenance organization (HMO) or other prepaid practice plan, and faculty practice plan.

Table 5.4. Naïve and bivariate probit analyses for potentially inappropriate antidepressant prescriptions among older adults in office-based primary care outpatient settings, NAMCS 2010-2012.

	Naïve probit model for potentially inappropriate antidepressant prescriptions			Bivariate probit model					
				Model for depression screening			Model for potentially inappropriate antidepressant prescriptions		
Variables (Reference group in parenthesis)	b	95% CI	*P*-value	b	95% CI	*P*-value	b	95% CI	*P*-value
Depression screening (No)									
Yes	**-0.95**	**-1.46 - -0.44**	**<0.001**	-	-	-	**-2.17**	**-2.80 - -1.53**	**<0.001**
Diagnosis of mood disorders[a)] (No/missing)									
Yes	-0.11	-0.39 - 0.18	0.469	0.53	0.31 - 0.75	<0.001	0.07	-0.43 - 0.57	0.772
Age (65-74)									
75-84	-0.15	-0.37 - 0.08	0.197	0.05	-0.13 - 0.22	0.585	-0.12	-0.33 - 0.08	0.239
85+	-0.56	-0.84 - -0.29	<0.001	-0.07	-0.33 - 0.19	0.607	-0.51	-0.83 - -0.18	0.002
Gender (Male)									
Female	0.27	0.06 - 0.49	0.012	0.04	-0.13 - 0.21	0.668	0.25	0.04 - 0.46	0.020
Race/ethnicity (Non-Hispanic White)									
Non-Hispanic Black	-0.23	-0.64 - 0.18	0.265	0.17	-0.24 - 0.58	0.419	-0.16	-0.55 - 0.23	0.432
Hispanic	0.00	-0.37 - 0.37	1.000	0.18	-0.21 - 0.56	0.378	0.04	-0.34 - 0.42	0.842
Others[b)]	0.39	-0.19 - 0.98	0.189	-0.32	-0.82 - 0.19	0.216	0.25	-0.54 - 1.05	0.532
Region (Northeast)									
Midwest	-0.17	-0.44 - 0.09	0.201	0.00	-0.33 - 0.34	0.988	-0.14	-0.41 - 0.12	0.293
South	0.09	-0.15 - 0.33	0.485	0.36	0.05 - 0.66	0.022	0.16	-0.12 - 0.44	0.266
West	-0.16	-0.44 - 0.12	0.258	0.20	-0.17 - 0.56	0.289	-0.09	-0.44 - 0.27	0.636
Source of payment (Medicare)									
Private	-0.02	-0.31 - 0.27	0.893	-0.10	-0.39 - 0.19	0.490	-0.04	-0.31 - 0.24	0.783
Medicaid	0.34	-0.19 - 0.87	0.208	-0.32	-0.90 - 0.26	0.280	0.22	-0.38 - 0.82	0.472
Others[c)]	-0.14	-0.69 - 0.40	0.602	-0.41	-1.08 - 0.25	0.223	-0.14	-0.61 - 0.33	0.557
Reason for visit (Acute problem)									
Routine chronic problem	-0.01	-0.23 - 0.21	0.934	0.06	-0.17 - 0.30	0.597	0.01	-0.21 - 0.22	0.960
Preventive care	-0.17	-0.46 - 0.12	0.250	0.36	0.09 - 0.64	0.010	0.58	-0..05 - 1.22	0.073
Pre- or post-surgery	0.70	0.24 - 1.15	0.003	-0.48	-1.14 - 0.18	0.151	-0.03	-0.43 - 0.37	0.876
Repeat of visits (None)									
1-2 visits	-0.16	-0.66 - 0.35	0.543	-0.18	-0.50 - 0.13	0.257	-0.18	-0.63 - 0.27	0.427
3-5 visits	0.08	-0.40 - 0.56	0.743	-0.15	-0.41 - 0.11	0.255	0.03	-0.42 - 0.48	0.890
6+ visits	-0.24	-0.73 - 0.24	0.322	-0.38	-0.72 - -0.05	0.026	-0.29	-0.74 - 0.15	0.199

Type of medical practice (Solo)									
Others[d)]	-0.14	-0.43 - 0.15	0.355	0.12	-0.21 - 0.45	0.479	-0.07	-0.40 - 0.25	0.660
MSA status (MSA)									
Non-MSA	0.14	-0.07 - 0.35	0.196	-0.40	-0.68 - -0.11	0.006	0.03	-0.29 - 0.35	0.840
Time spent with doctor (< 15 min.)									
15-20 min.	0.15	-0.18 - 0.48	0.375	-0.15	-0.42 - 0.11	0.265	0.12	-0.17 - 0.42	0.417
21-30 min.	0.22	-0.16 - 0.60	0.256	0.07	-0.15 - 0.28	0.535	0.23	-0.10 - 0.58	0.173
> 30 min.	0.25	-0.12 - 0.62	0.187	0.07	0.22 - 0.37	0.618	0.24	-0.11 - 0.60	0.175
Multiple chronic conditions (MCCs) (None)									
1	0.00	-0.36 - 0.37	0.985	0.14	-0.29 - 0.57	0.527	0.04	-0.31 - 0.40	0.809
2-3	-0.21	-0.56 - 0.14	0.236	0.33	-0.12 - 0.77	0.151	-0.10	-0.55 - 0.34	0.649
4+	-0.32	-0.65 - 0.02	0.067	0.64	0.20 - 1.08	0.004	-0.13	-0.66 - 0.40	0.634
Number of medications (0-2)									
3-5	1.08	0.64 - 1.52	<0.001	0.10	-0.16 - 0.36	0.446	0.91	0.17 - 1.65	0.016
6+	1.42	1.01 - 1.84	<0.001	0.13	-0.10 - 0.37	0.258	1.22	0.39 - 2.05	0.004
Psychiatric services (No)									
Yes	-0.02	-0.89 - 0.86	0.972	1.06	0.46 - 1.66	0.001	0.55	-0.60 - 1.70	0.347
Injury prevention (No)									
Yes	-	-	-	**0.61**	**0.19 - 1.03**	**0.005**	-	-	-
Stress management (No)									
Yes	-	-	-	**0.75**	**0.32 - 1.18**	**0.001**	-	-	-

Note: rho = 0.33; p<0.001. a) refers to appendix 5.1; b)includes Asians, American Indian/Alaska Natives (AIANs), Native Hawaiian or Other Pacific Islanders (NHOPI), and multiple races; c) includes worker's compensation, self-pay, no charge, and others; and d) includes federally qualified health center (FQHC), non-federal government clinic, family planning clinic, health maintenance organization (HMO) or other prepaid practice plan, and faculty practice plan.

Appendix 5.1. Mental health diagnosis[28]

Diagnosis	ICD-9-CM diagnostic code (290-319)
Affective disorder	
Major depression	296.2 & 296.3
Dysthymia	300.4
Other affective disorder	296.1, 296.81, 296.82, 296.9, & 311.0
Bipolar disorder	
Bipolar disorder	296.00-296.06, 296.40-296.46, 296.50-296.56, 296.60-296.66, 296.7, 296.80, 296.89
Schizophrenia	
Schizophrenia	295
Delirium, dementia, and other cognitive impairment	
Delirium	290.11, 290.3, 290.41, 291.0, 292.81, 293.0, 293.1
Dementia and other cognitive impairment	290, 291.2, 292.82, 294.10, 294.11, 294.20, 294.21, 331.0, 331.19, 331.82, 331.83
Anxiety Disorders	
Generalized anxiety disorder (GAD)	300.02
Panic disorder with or without agoraphobia	300.01 & 300.21
Obsessive-compulsive disorder	300.3
Personality Disorders	
Personality disorders	301
Others	Otherwise

Appendix 5.2. Antidepressant medications by class[29]

Tricyclics (TCAs)
- Amitriptyline[a), b), f)]
- Amoxapine[b)]
- Clomipramine[a), b), f)]
- Desipramine[b)]
- Doxepin[a), b), f)]
- Imipramine[a), b), f)]
- Maprotiline
- Nortriptyline[b)]
- Protriptyline[b)]
- Trimipramine[a), b), f)]

Serotonin Modulators
- Nefazodone
- Trazodone
- Vilazodone[e)]
- Vortioxetine[e)]

Selective Serotonin Reuptake Inhibitors (SSRIs)
- Citalopram
- Escitalopram
- Fluoxetine
- Fluvoxamine
- Paroxetine[b)]
- Sertraline

Monoamine Oxidase Inhibitors (MAOIs)
- Isocarboxazid
- Phenelzine
- Tranylcypromine
- Rasagiline[c)]
- Selegiline[c)]

Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)
- Desvenlafaxine
- Duloxetine
- Levomilnacipran[e)]
- Venlafaxine
- Milnacipran[d)]

Miscellaneous
- Bupropion
- Mirtazapine

Note: a) denotes tertiary TCAs; b) denotes drugs with strong anticholinergic properties; c) denotes a MAO-B inhibitor and is primarily classified as anti-Parkinsonian agents; d) is primarily classified as fibromyalgia agents; e) indicates that it is not available in NAMCS; and f) indicates that it should be avoided, regardless of diagnosis, according to 2012 Beers criteria.

Appendix 5.3. 2012/2015 Beers criteria for potentially inappropriate antidepressant use in older adults due to drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome[14]

Disease or syndrome (ICD-9-CM code)	Antidepressant[a)]	Rationale	Recommendation	Quality of Evidence	Strength of recommendation
Cardiovascular					
Syncope (780.2, 992.1)	Tertiary TCAs	Increase risk of orthostatic hypotension or bradycardia	Avoid	Moderate	Strong
Central nervous system					
Chronic seizures or epilepsy (345, 780.33)	bupropion; maprotiline	Lowers seizure threshold; may be acceptable in patients with well-controlled seizures in whom alternative agents have not been effective	Avoid	Moderate	Strong
Delirium (290.11, 290.3, 290.41, 291.0, 292.81, 293.0, 293.1)	TCAs; Anticholinergics	Induce or worsen delirium in older adults; if discontinuing drugs used chronically, taper to avoid withdrawal symptoms	Avoid	Moderate	Strong
Dementia and cognitive impairment (290, 291.2, 292.82, 294.10, 294.11, 294.20, 294.21, 331.0, 331.19, 331.82, 331.83)	Anticholinergics	Avoid because of adverse CNS effects	Avoid	High	Strong
History of falls or fractures (E880-E888)[b)]	TCAs; SSRIs	Ability to produce ataxia, impaired psychomotor function, syncope, and additional falls	Avoid unless safer alternatives are not available	High	Strong
Gastrointestinal					
Chronic constipation (564)	Tertiary TCAs; Anticholinergics	Can worsen constipation	Avoid unless no other alternatives	Moderate to low	Weak
Lower urinary tract symptoms, benign prostatic hyperplasia (600)	Anticholinergics	May decrease urinary flow and cause urinary retention	Avoid in men	Moderate	Inhaled agents: strong; others: weak

Note: a) refers to appendix 5.1 for full description; and b) excluded in the analysis for consistency, as NAMCS only collected external cause information using ICD-9-CM in 2002-2004.

CHAPTER 6

Conclusion

6.1 Summary of findings

The three essays on potentially inappropriate antidepressant use among older adults in their office-based outpatient visits employ three different methodological approaches: health services epidemiology (chapter 3), policy impact evaluation (chapter 4), and clinical practice evaluation (chapter 5). Each essay presents its unique research questions with rationale (i.e., gaps in literature). Findings and implications of these essays are summarized in Table 6.1.

6.2. Strengths and limitations

One of strengths in these essays is the use of data from NAMCS, which provides a unique opportunity to explore issues surrounding overall and potentially inappropriate antidepressant prescriptions in a nationally-representative sample of U.S. older adults in office-based outpatient settings. However, using data from the NAMCS also includes several limitations. For example, across the three essays, one limitation is that NAMCS only collected up to three diagnoses in a sampled visit and it might have resulted in under-representation of potentially inappropriate antidepressant prescriptions. Each essay should be interpreted carefully with its strengths and limitations.

Table 6.1. Summary of findings

Title	Rationale	Finding
Chapter 3 (manuscript #1): Potentially Inappropriate Antidepressant Use among Older Adults in Office-based Outpatient Settings: National Trends from 2002 to 2012	• A Beers criterion is continuously updated over time, but we do not know descriptive patterns of potentially inappropriate antidepressant prescriptions in U.S. older adults. • **Objectives**: To estimate the prevalence of two outcomes (i.e., overall and potentially inappropriate antidepressant prescriptions), and to investigate demographic and clinical factors associated with these outcomes among adults ages 65 and older in their office-based outpatient visits.	• The prevalence of overall antidepressant prescriptions increase almost twofold from 5.2% in 2002 to 10.1% in 2012. • About one in 10 older adults with antidepressant-related visits are exposed to the potentially inappropriate antidepressant prescriptions. • Amitriptyline and doxepin are accounted for more than 70% of potentially inappropriate antidepressants. • **Conclusion**: Potentially inappropriate antidepressant prescriptions remain a serious problem in office-based outpatient visits. Efforts to minimize potentially inappropriate antidepressant use are needed by targeting specific disease-independent antidepressant agents (e.g., amitriptyline and doxepin).
Chapter 4 (manuscript #2): Impacts of the 2009 USPSTF Depression Screening Recommendation: A Difference-in-Differences Analysis	• In primary care settings, depression screening is provided to detect and treat untreated depression and other related mood disorders. The United States Preventive Services Task Force (USPSTF) updated its depression guideline in 2009, but relatively little is known about its impact on outcomes (see below) among older adults in office-based primary care outpatient settings. • **Objectives**: To examine the impact of the 2009 USPSTF depression screening recommendation on the following outcomes: diagnoses of depression and other mood disorders; antidepressant prescriptions; and provision of non-pharmacological psychiatric services among older adults ages 65 and over in their office-based primary care outpatient visits.	• Prevalence of visits associated with the diagnosis of mood disorders other than depression differentially decreased by 18.8 percentage points (95% CI: -31.1, -6.5; p=0.003). • No differential impact was found in other outcomes. • **Conclusion**: The 2009 USPSTF depression screening recommendation resulted in a decreased rate of diagnosing mood disorders other than depression, but had no impact on prescribing patterns of antidepressants or provision of non-pharmacological psychiatric services among older adults ages 65 and over in their office-based primary care outpatient visits.

Title	Rationale	Finding
Chapter 5 (manuscript #3): Effects of Depression Screening on Diagnosing and Treating Mood Disorders among Older Adults in Office-based Primary Care Outpatient Settings: An Instrumental Variable Analysis	• The 2009 USPSTF depression screening recommendation had no impact on potentially inappropriate antidepressant prescriptions (see Chapter 4). It is of question if depression screening should still be provided in clinical practice in primary care settings. • **Objectives**: To examine the effects of depression screening on three outcomes: diagnosis of mood disorders, overall antidepressant prescriptions, and potentially inappropriate antidepressant prescriptions, when controlled for policy initiative (i.e., post-2009 USPSTF depression screening recommendation era) and other covariates.	• No significant effect of depression screening on diagnosis of mood disorders or overall antidepressant prescriptions was found. • Depression screening was negatively associated with potentially inappropriate antidepressant prescriptions (B=-2.17; 95% CI: -2.80, -1.53; $p<0.001$). • **Conclusion**: Using an instrumental variable technique, which accounts for omitted variable bias and over-identification issues, depression screening had a negative effect on potentially inappropriate antidepressant prescriptions. While both policy and practice modifications with respect to depression screening would require further research, primary care healthcare providers should actively utilize depression screening along with their judgment calls to provide the best available mental health care to older adult patients in their visits.

6.3. Future research

The ultimate goal of this project is to bring positive impact by promoting clinical and policy efforts to improve patient safety in older adults who are prescribed with antidepressants in office-based outpatient settings. As shown in chapter 3, potentially inappropriate antidepressant prescriptions remain a serious problem in office-based outpatient visits. Because amitriptyline and doxepin are two disease- or syndrome-independent agents that together accounted for more than 70% of potentially inappropriate antidepressant prescriptions, practice interventions for minimizing the use of these two antidepressant agents should be considered for older adult patients in office-based outpatient settings.

In addition, depression screening was found to have promising impacts on potentially inappropriate antidepressant prescriptions, as shown in chapters 4 and 5. According to findings from chapter 4, which focuses on policy impact evaluation, no impact of depression screening on potentially inappropriate antidepressant prescription was found due to the 2009 USPSTF depression screening initiative. Unlike this finding, however, depression screening was negatively associated with potentially inappropriate antidepressant prescriptions in clinical practice evaluation. These findings suggest that while both policy and practice modifications with respect to depression screening would require further research (e.g., standardization of depression screening tools for older adult patients), primary care healthcare providers should actively utilize depression screening along with their judgment calls to provide the best available mental health care to older adult patients in their primary care visits.

CHAPTER 7

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